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RESEARCH**

APPLICATION NUMBER:
200153Orig1s000

PROPRIETARY NAME REVIEW(S)

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

Proprietary Name Review

Date: April 26, 2013

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Drug Name and Strength(s): Liptruzet (Ezetimibe and Atorvastatin) Tablets,
10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, and 10 mg/80 mg

Application Type/Number: NDA 200153

Applicant/Sponsor: Merck

OSE RCM #: 2013-569

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Liptruzet, 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

The Applicant, Merck, initially submitted the proposed proprietary name request for Atozet for our review on July 7, 2011 as part of the NDA. The proposed proprietary name, Atozet was found conditionally acceptable from a promotion and safety perspective by the Office of Prescription Drug Promotion (OPDP) and the Division of Medication Error Prevention and Analysis (DMEPA), respectively in OSE Review #2011-2469 dated September 26, 2011. On February 29, 2012, the application received a Complete Response (CR) Letter due to bioequivalence issues.

On December 14, 2012, Merck resubmitted the NDA and the request for review of the proposed proprietary name, Atozet to the NDA, and stated that none of the product characteristics has changed. The proposed proprietary name, Atozet was found unacceptable due to sound alike and product characteristic similarities with a currently marketed product, Aricept in OSE #2012-2940, dated February 19, 2013. These findings were also communicated with Merck via a teleconference call on February 19, 2013. Subsequently, Merck submitted a request for review of an alternate proprietary name, Liptruzet on February 25, 2013.

1.2 PRODUCT INFORMATION

The following product information is provided in the February 25, 2013 proprietary name submission.

- Active Ingredient: Ezetimibe and Atorvastatin
- Indication: For reduction of cholesterol in primary hyperlipidemia and homozygous familial hypercholesterolemia.
- Route: Oral
- Dosage Form: Tablets
- Strengths: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg
- Dose and Frequency: One tablet by mouth once daily
- How Supplied: Physician Sample carton containing 3 pouches with each pouch containing 7 tablets; Trade Carton containing 9 pouches with each Trade Foil Pouch of 10 tablets
- Storage: Store at 20-25°C (68-77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]
- Container and Closure Systems: The drug product will be packaged in a vented (b) (4) blister with push-through aluminum lidding. The (b) (4) aluminum blister card is enclosed in a (b) (4) plastic case (for child

resistance) which is contained in a (b) (4) aluminum pouch along with 2 oxygen scavengers and one (b) (4) desiccant canister.

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 Metabolism and Endocrinology Products 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

The March 4, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Liptruzet, is a coined term with no intrinsic meaning. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error. However, we note that components of the proposed proprietary name, Liptruzet, are made up of the two active ingredients, Lipitor and Zetia (i.e. "Lip" from Lipitor (atorvastatin) and "zet" from Zetia (ezetimibe)). We do not find this name misleading because it suggests both active ingredients in the proposed proprietary name.

In addition, we also note that the established name is presented as Ezetimibe and Atorvastatin. On April 2, 2013, we consulted with CMC to ensure that the name sequence is acceptable since it is not presented in alphabetical order. CMC agrees with the established name presentation (Ezetimibe and Atorvastatin). The rationale is that for combination products, the order of the established names is determined by the relative strengths of the individual active ingredients in the product. In this case, the dose of ezetimibe is fixed at 10 mg and the dose of atorvastatin ranges from 10 mg to 80 mg. Therefore, since the strength(s) of atorvastatin is greater than the strength of ezetimibe, the name of the drug would be ezetimibe and atorvastatin. Also, this presentation is consistent with the other ezetimibe and statin combination product, Vytorin (Ezetimibe and Simvastatin).

We also reviewed the name for similarity to Lipitor and those findings are discussed in Appendix E.

2.2.3 FDA Name Simulation Studies

Seventy-nine practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Nineteen of the 27 inpatient participants responded correctly and the most common misinterpretation occurred with 5 participants misinterpreting the letter 'u' for 'a' (i.e. 'LiptrUzet' misinterpreted as "Liptrazet"). Two of the 23 voice participants responded correctly and a common misinterpretation occurred with participants misinterpreting the letter 'u' for 'i' (i.e. 'LiptrUzet' misinterpreted as "Liptrizet" n=8, "Liptriset" n=1 and Liptricept n=1). Fourteen of the 29 outpatient participants responded correctly and the most common misinterpretation occurred with 7 participants misinterpreting the letter 'u' for 'i' (i.e. 'LiptrUzet' misinterpreted as "Liptrizit" n=4 and Liptrizit" n=3). We have considered these variations in our look-alike and sound-alike searches and analysis. See Appendix C for the complete listing of interpretation from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, March 18, 2013 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not have any objections to the proposed name at the initial phase of the proprietary name review.

2.2.5 External Proprietary Name Risk Assessment

The external proprietary name risk assessment was conducted by (b) (4). The study report is dated March 4, 2011 and submitted on March 6, 2013. In the report, (b) (4) did not identify notable look-alike and sound-alike names to Liptruzet. However, they identified a concern regarding the "Lip" letter string that begins both Lipitor and Liptruzet during computerized order entry. The report notes that practitioners may enter the first three letters of either medication plus the strength or a portion of the strength (i.e. Lip 10) and the wrong product may be inadvertently selected and dispensed in error. According to the Institute of Safe Medication Practices Guidelines on Standard Order Sets, which applies to both printed and electronic formats, drug names should be presented as the generic name, followed by brand name when appropriate¹. In this case, if a prescriber enters LIP10 during computerized physician order entry (CPOE), options will include both "atorvastatin (Lipitor)" as well as "ezetimibe and atorvastatin (Liptruzet), thus will help the prescriber choose the appropriate product. By providing the established name, it helps in differentiating the two products and prevents or mitigates prescribing errors when using CPOE. In addition, Lipitor is a single ingredient product and its strength will be presented as 10 mg, 20 mg, 40 mg, and 80 mg) versus Liptruzet is a combination product and we think it is likely that electronic systems will display both strengths (i.e. 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, and 10 mg/80 mg). We also note that there are other currently marketed products whose names begin with "Lip" (i.e. Lipotriad, Liposyn, Lipodox, and Lipistart). In some instances, these products do have numerical overlap with Lipitor e.g. Liposyn (Fat Emulsion), which is available in 10%, 20%, and 30% strengths. However, we are not aware of confusion or medication error cases involving Liposyn and Lipitor. Therefore, in our assessment of the concern regarding the "Lip" letter string that begins

¹ <http://www.ismp.org/Tools/guidelines/StandardOrderSets.asp>. Accessed April 16, 2013

both Lipitor and Liptruzet during computerized order entry we find that the aforementioned combination of factors is expected to minimize the risk of selection error between these two names and would not pose a risk for confusion.

2.2.6 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, Liptruzet. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Liptruzet identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

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>
Linjeta ^{***}	EPD	Letrozole	EPD	Ultracet	EPD
Lysteda	EPD	Lipotriad	EPD	Citrucel	EPD
Lipofen	EPD	Liposyn III	EPD	Lotronex	EPD
Lipidil	EPD	Lupaneta Pack	EPD	Lipitor	EPD
Intralipid	EPD	Lipodox	EPD	Zuplenz	EPD
Cystospaz	EPD	Lipistart	EPD	Lapatinib	EPD
Look and Sound Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Liptruzet	EPD	Liquicet	EPD		

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

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products via e-mail on March 27, 2013. At that time we also requested additional

^{***} This is proprietary and confidential information that should not be released to the public

information or concerns that could inform our review. Per e-mail correspondence from the Division of Metabolism and Endocrinology Products on March 27, 2013, they stated no additional concerns with the proposed proprietary name, Liptruzet.

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 Margarita Tossa, OSE project manager, at 301-796-4053

3.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The results are subject to change. If any of the proposed product characteristics as stated in your February 25, 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 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.

² National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

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).

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

Type of Similarity	Considerations when Searching the Databases		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
	Similar spelling	Identical prefix 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

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Look-alike			<ul style="list-style-type: none"> 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 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

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

practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

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

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

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

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

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

- a. 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, Liptruzet	Scripted May Appear as	Spoken May Be Interpreted as
'L'	Z, S, T, V, d	w
lowercase 'l'	b, e, s, A, P, i	
lowercase 'i'	e, l, j	
lowercase 'p'	yn, ys, g, j, q	b
lowercase 't'	r, f, x, l	d
lowercase 'r'	s, n, e, v, u	
lowercase 'u'	n, y, v, w, a, i	y, i
lowercase 'z'	c, e, g, n, m, q, r, s, v, y	c, s, x
lowercase 'e'	a, i, l, o, u, p, c	i, y
lowercase 't'	r, f, x, l	d, pt
Letter Strings		
Li	U, V, b, h	
'tr'	H	
'ru'	M	
'ze'	U	
'et'	D	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Liptruzet Study (Conducted on March 7, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> <p>Liptruzet 10mg/20mg 1 tab p. daily</p>	<p>Liptruzet 10 mg/20 mg One tab by mouth once daily</p>
<p><u>Outpatient Prescription:</u></p> <p>Liptruzet 10mg/20mg #30 1 po qday</p>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

191 People Received Study

79 People Responded

Total	27	23	29	
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
(b) (4)	1	0	0	1
LIFTUZET	0	1	0	1
LIPRITREX	0	1	0	1
LIPTMRET	0	0	1	1
LIPTRAZET	5	1	0	6
LIPTREZET	0	0	2	2
LIPTRICEPT	0	1	0	1
LIPTRISSET	0	1	0	1
LIPTRIZET	0	8	3	11
LIPTRIZIT	0	0	4	4
LIPTROSET	0	1	0	1
LIPTRROUT	0	0	1	1

LIPTROZET	2	1	1	4
LIPTROZETTE	0	1	0	1
LIPTRUCET	0	1	0	1
LIPTRUSET	0	2	0	2
LIPTRUSETTE	0	1	0	1
LIPTRUZET	19	2	13	34
LIPTRUZET 10MG/20MG	0	0	1	1
LIPTRUZIT	0	0	3	3
LIPTUSET	0	1	0	1

(b) (4)

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

Proprietary Name		Active Ingredient	Similarity to Liptruzet	Failure preventions
1	Linjeta ***	Monomeric Recombinant Human Insulin	Look alike	This proposed name was found unacceptable in OSE #2012-1369.
2	Lysteda	Tranexamic Acid	Look alike	The pair has sufficient orthographic differences.
3	Lipofen	Fenofibrate	Look alike	The pair has sufficient orthographic differences.
4	Lipidil	Fenofibrate	Look alike	The pair has sufficient orthographic differences.
5	Intralipid	Fat Emulsion	Look alike	The pair has sufficient orthographic differences.
6	Liptruzet	Atorvastatin and Ezetimibe	Look and sound alike	This name is the subject of this review.

*** This is 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.

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>1</p>	<p>Ultracet (Acetaminophen and Tramadol)</p> <p>Dosage Form and Strength: Fixed dose combination Oral tablets: 325 mg/37.5 mg</p> <p>Usual dose: 2 tablets by mouth every 4 to 6 hours as needed</p>	<p>Orthographic similarity: The beginning letter string ‘Li’ and ‘U,’ ‘u’ and ‘a,’ and ‘z’ and ‘e’ appear orthographically similar when scripted. Both names contain the infix letter string ‘tr’ in similar positions and end with the letter string ‘et’</p> <p>Dosage form and route of administration: Both are available as oral tablets.</p>	<p>Orthographic difference: Liptruzet contains a downstroke ‘p’ in the same position as the upstroke ‘l’ in Ultracet, giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Liptruzet will require strength as it is available in multiple strengths vs. Ultracet is available in single strength and may be omitted. There is no numerical overlap or similarity between the strengths.</p> <p>Frequency: Liptruzet is prescribed once daily vs. Ultracet is prescribed every 4 to 6 hours as needed.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
2	<p>Citrucel (Methylcellulose)</p> <p>Dosage Form and Strength: Oral powder: 2 gm/10.7 gm</p> <p>Usual dose: 1 heaping tablespoon (19 gm) or 1 packet in 8 oz cold water, 1 to 3 times daily.</p>	<p>Orthographic similarity: The beginning letter ‘L’ and ‘C’ and ending letter ‘t’ and ‘l’ appear orthographically similar when scripted. Both names contain the letter string ‘truce’ in similar positions.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p> <p>Frequency: Both Liptruzet and Citrucel may be prescribed once daily.</p>	<p>Orthographic difference: Liptruzet contains a downstroke ‘p’ in position 3 which is absent in Citrucel, giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Liptruzet will require strength as it is available in multiple strengths vs. Citrucel is available in single strength and may be omitted. There is no numerical overlap or similarity between the strengths.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
3	<p>Lotronex (Alosetron HCl)</p> <p>Dosage Form and Strength: Oral tablets: 0.5 mg and 1 mg</p> <p>Usual dose: 0.5 mg by mouth twice daily, up to 1 mg twice daily.</p>	<p>Orthographic similarity: Both names begin with the letter ‘L’ and contain the infix letter string ‘tr’ in similar positions. In addition, the ending letter strings ‘zet’ and ‘nex’ appear orthographically similar when scripted.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p> <p>Strength: Both are available in multiple strengths and there is numerical similarity between the two strengths (<i>i.e.</i> 10 mg vs. 1 mg)</p>	<p>Orthographic difference: Liptruzet contains a downstroke ‘p’ in position 3 which is absent in Citrucel, giving the names different shapes. In addition, the second letter ‘i’ and ‘o’ appear orthographically different when scripted.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
4	<p>Lipitor (Atorvastatin)</p> <p>Dosage Form and Strength: Oral tablets: 10 mg, 20 mg, 40 mg, and 80 mg</p> <p>Usual dose: 1 tablet by mouth once daily.</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Lip’ and contain a cross stroke ‘t’ in similar positions.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p> <p>Strength: Both Liptruzet and Lipitor are available in multiple strengths. Although Liptruzet is a combination product, the Ezetimibe strength is constant thus may be considered a complete prescription when written with only the Atorvastatin strength (10 mg, 20 mg, 40 mg, and 80 mg). There is numerical overlap between the two strengths during prescription writing (<i>i.e.</i> 10 mg, 20 mg, 40 mg and 80 mg)</p> <p>Frequency: Both are prescribed as once daily.</p>	<p>Orthographic difference: Liptruzet (9 letters) appears orthographically longer than Lipitor (7 letters) when scripted. In addition, Liptruzet contains an additional cross stroke ‘t’ at the end of the name which is absent in Lipitor, giving the names different shapes.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
5	<p>Liquicet (Acetaminophen and Hydrocodone Bitartrate)</p> <p>Dosage Form and Strength: Oral solution: 500 mg/10 mg per 5 mL</p> <p>Usual dose: 5 to 15 mL by mouth every 4 to 6 hours as needed</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Li’ and end with the letter string ‘e.’ In addition, the letters ‘p’ and ‘q’ in position 3 and the letter string ‘ruz’ and ‘uic’ appear orthographically similar when scripted.</p> <p>Phonetic similarity: Both names contain three syllables. The first syllables ‘Lip’ and Liq’ and the last syllable ‘zet’ and ‘cet’ sound phonetically similar when spoken.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p> <p>Dose and units of measure: There is numerical overlap between doses during written prescription (<i>i.e.</i> 10 mg vs. 10 mL).</p>	<p>Orthographic difference: Liptruzet contains an upstroke ‘t’ in position 4 which is absent in Liquicet, giving the names different shapes.</p> <p>Phonetic difference: The second syllable ‘tru’ and ‘ui -/we/’ sound phonetically different when scripted. In addition, the dose for Liptruzet and Liquicet sound different when ordered verbally (<i>i.e.</i> Liptruzet 10 mg vs. Liquicet 10 mL or 2 teaspoons).</p> <p>Frequency: Liptruzet is prescribed as once daily vs. Liquicet is prescribed every 4 to 6 hours as needed.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
6	<p>Letrozole</p> <p>Dosage Form and Strength: Oral tablets: 2.5 mg</p> <p>Usual dose: 1 tablet by mouth once daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Li’ and ‘Le,’ the infix letter strings ‘tru’ and ‘tro’, and ending letter strings ‘zet’ and ‘zol’ appear orthographically similar when scripted.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p> <p>Frequency: Both are prescribed as once daily.</p>	<p>Orthographic difference: Liptruzet contains a downstroke ‘p’ in position 3 which is absent in Letrozole, giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Liptruzet will require strength as it is available in multiple strengths vs. Letrozole is available in single strength and may be omitted. There is no numerical overlap or numerical similarity in strengths.</p>
7	<p>Lipotriad (Vitamin B Complex, Vitamin C, Biotin, and Folic Acid)</p> <p>Dosage Form and Strength: Oral tablet</p> <p>Usual dose: 1 tablet by mouth once daily</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Lip’ and contain the letter string ‘tr’ in similar positions. In addition, the ending letter string ‘et’ and ‘d’ appear orthographically similar when scripted.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p> <p>Frequency: Both are prescribed as once daily</p>	<p>Orthographic difference: Lipotriad contains an additional letter ‘o’ between the downstroke ‘p’ and upstroke ‘t’ giving the names different shapes. In addition, the letter strings ‘uz’ and ‘ia’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Liptruzet will require strength as it is available in multiple strengths vs. Lipotriad is available in single strength combination and may be omitted.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
8	<p>Liposyn III (Fat Emulsion)</p> <p>Dosage Form and Strength: Injection, emulsion: 10%, 20%, 30%</p> <p>Usual dose: 1 gm/kg/day (not to exceed 500 mL 20% fat emulsion on the first day of therapy), increase by 1 gm/kg/day to a maximum of 2.5 g/kg/day. Based on 70 kg adult: 70 gm, up to a maximum of 175 gm</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Lip’</p> <p>Strength: Both Liptruzet and Liposyn are available in multiple strengths. Although Liptruzet is a combination product, the Ezetimibe strength is constant thus may be considered a complete prescription when written with only the Atorvastatin strength (10 mg, 20 mg, 40 mg, and 80 mg). There is numerical overlap between the two strengths during prescription writing (<i>i.e.</i> 10 mg vs. 10 %, 20 mg vs. 20 %)</p> <p>Frequency: Both may be prescribed once daily.</p>	<p>Orthographic difference: Liptruzet contains a upstroke ‘t’ in positions 4 and 9 which is absent in Liposyn giving the names different shapes.</p> <p>Dose: 1 tablet vs. 1 gm/kg/day to 2.5 g/kg/day</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
9	<p>Lupaneta Pack (Leuprolide and Norethindrone)</p> <p>Dosage Form and Strength: Injectable and oral tablet: 3.75 mg/vial and 5 mg; 11.25 mg and 5 mg</p> <p>Usual dose: -Lupron Depot 3.75 mg for 1-month administration given as a single intramuscular injection every 1 month, and Norethindrone Acetate 5 mg Tablets taken orally once per day for one month; -Lupron Depot 11.25 mg for 3-month administration given as a single intramuscular injection once every 3 months, and Norethindrone 5 mg tablets taken orally once per day for 3 months.</p>	<p>Orthographic similarity: The beginning letter strings ‘Lip’ and ‘Lup’ appear orthographically similar when scripted.</p>	<p>Orthographic difference: Liptruzet contains a upstroke ‘t’ in positions 4 and 9 versus Lupaneta contains a cross stroke in position 7, giving the names different shapes.</p> <p>Strength: Both are available in multiple strengths which need to be specified for a complete prescription. There is no numerical overlap or numerical similarity between the strengths.</p> <p>Frequency: Liptruzet is prescribed once daily vs. Lupaneta is prescribed either once monthly or every 3 months.</p> <p>Dose and units of measure: 1 tablet vs. 3.75 mg and 5 mg or 11.25 and 5 mg or as directed</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
10	<p>Lipodox (Doxorubicin HCl Liposomal)</p> <p>Dosage Form and Strength: Intravenous injection 2 mg/mL</p> <p>Usual dose: 20 mg/m² intravenously at an initial rate of 1 mg/min to minimize the risk of infusion-related reactions. If no infusion-related adverse reactions are observed, the infusion rate should be increased to complete the administration of the drug over 1 hour. Repeat once every 3 weeks. Based on Average Adult BSA (1.72 m²) dose is 34.4 mg.</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Lip’</p> <p>Strength and Dose: Although Liptruzet is a combination product, the Ezetimibe strength is constant thus may be considered a complete prescription when written with only the Atorvastatin strength (10 mg, 20 mg, 40 mg, and 80 mg) and Lipodox is calculated based on BSA. Thus, there may be a numerical overlap between the strength of Liptruzet and dose of Lipodox (<i>i.e.</i> 20 mg, 40 mg).</p>	<p>Orthographic difference: Liptruzet (9 letters) appear orthographically longer than Lipodox (7 letters). In addition, Liptruzet contains an upstroke ‘t’ in position 4 and 9 which is absent in Lipodox and Lipodox contains an upstroke ‘d’ in position 5 which is absent in Liptruzet, giving the names different shapes.</p> <p>Frequency: Liptruzet is prescribed once daily vs. Lipodox is prescribed once or now.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
11	<p>Zuplenz (Ondansetron)</p> <p>Dosage Form and Strength: Oral film: 4 mg and 8 mg</p> <p>Usual dose: 8 mg by mouth 3 times daily; 24 mg by mouth, given 30 minutes before chemotherapy</p>	<p>Orthographic similarity: The beginning letter string ‘Lip’ and ‘Sup’ appear orthographically similar when scripted. In addition, both names contain a cross stroke/upstroke ‘t’ and ‘l’ and the letter ‘z’ in similar position.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: Liptruzet (9 letters) contains additional letters ‘et’ after the letter ‘z’ which makes it orthographically longer than Zuplenz (7 letters).</p> <p>Strength: Both are available in multiple strengths which need to be specified for a complete prescription. There is no numerical overlap or numerical similarity between the strengths.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
12	<p>Cystospaz* and Cystospaz-M (Hyoscyamine Sulfate)</p> <p>Dosage Form and Strength: Oral Tablet: 0.15 mg M- Extended-release capsule: 0.375 mg</p> <p>Usual dose: Adults, Adolescents, and Children greater than 12 years: 0.125 mg to 0.25 mg by mouth every 4 hours or as needed. Maximum dosage is 1.5 mg/day. <i>Children 2 to 12 years:</i> 0.0625 mg to 0.125 mg by mouth every 4 hours or as needed. Maximum dosage is 0.75 mg/day</p> <p><i>M: Adults, Adolescents, and Children 12 years:</i> 0.375 mg to 0.75 mg by mouth every 12 hours or 0.375 mg by mouth every 8 hours. Maximum dosage is 1.5 mg/day. <i>Children 2—11 years:</i> 0.375 by mouth every 12 hours. Maximum dosage is 0.75 mg/day. <i>*Discontinued with generic available</i></p>	<p>Orthographic similarity: The beginning letter strings ‘Lipt’ and ‘Cyst’ appear orthographically similar when scripted. In addition, both names contain a downstroke ‘z’ and ‘p’ in similar positions.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: The infix letter strings ‘ru’ and ‘os’ appear orthographically different when scripted. In addition, Liptruzet contains a upstroke ‘t’ at the end of the name which is absent in Cystospaz, giving the names different shapes.</p> <p>Strength: Both are available in multiple strengths which need to be specified for a complete prescription. There is no numerical overlap or numerical similarity between the strengths.</p> <p>Frequency: Liptruzet is prescribed as once daily vs. Cystospaz is prescribed as every 4 hours or as needed.</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
13	<p>Lipistart (Whey protein, carbohydrate, fat (high in medium chain triglycerides (MCT) and low in long chain triglycerides (LCT)), vitamins, minerals and trace elements)</p> <p>Dosage Form and Strength: Oral powder: 5 gm per scoop</p> <p>Usual dose: Use as directed; The standard dilution of 15% (20kcal/fl oz) is made by adding 1 level scoop of (approx. 5g) to 30ml of water (approx. 1 fluid oz).</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Lip’ and end with the letter ‘t’</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p> <p>Frequency: Both may be prescribed as once daily</p>	<p>Orthographic difference: Liptruzet contains a upstroke ‘t’ in position 4 while Lipistart contains the upstroke ‘t’ in position 6, giving the names different shapes. In addition, Lipistart contains the letter string ‘is’ between the downstroke ‘p’ and upstroke ‘t’ which is absent in Liptruzet.</p> <p>Strength: Multiple vs. single. An order for Liptruzet will require strength as it is available in multiple strengths vs. Lipotriad does not have a strength.</p> <p>Dose: 1 tablet vs. Use as directed or 5 gm</p>

	<p>Proposed name: <i>Liptruzet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
14	<p>Lapatinib</p> <p>Dosage Form and Strength: Oral tablet: 250 mg</p> <p>Usual dose: - 1,250 mg (5 tablets) once daily on days 1 to 21 continuously in combination with capecitabine 2,000 mg/m²/day (administered orally in 2 doses approximately 12 hours apart) on days 1 to 14 in a repeating 21-day cycle; -1,500 mg once daily continuously in combination with letrozole 2.5 mg once daily</p>	<p>Orthographic similarity: The beginning letter string ‘Lip’ and ‘Lap’ appear orthographically similar when scripted.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p> <p>Frequency: Both may be prescribed as once daily</p>	<p>Orthographic difference: Liptruzet contains a upstroke ‘t’ in position 4 while Lapatinib contains the upstroke t in position 5 with the additional letter ‘a’ between the downstroke ‘p’ and upstroke ‘t’, giving the names different shapes. In addition, the ending letter strings ‘ruzet’ and ‘inib’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Liptruzet will require strength as it is available in multiple strengths vs. Lapatinib is available in single strength and may be omitted. There is no numerical overlap or similarity between the strengths.</p>

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/s/

REASOL AGUSTIN
04/26/2013

LUBNA A MERCHANT
04/26/2013

KELLIE A TAYLOR
04/26/2013

CAROL A HOLQUIST
04/26/2013

**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: February 19, 2013

Reviewer: Reasol S. Agustin, PharmD
Division of Medication Error Prevention and Analysis

Team Leader: Lubna Merchant, MS, PharmD
Division of Medication Error Prevention and Analysis

Deputy Director: Kellie Taylor, PharmD MPH
Division of Medication Error Prevention and Analysis

Division Director: Carol Holquist, RPh
Division of Medication Error Prevention and Analysis

Drug Name and Strength(s): Atozet (Ezetimibe and Atorvastatin) Tablets,
10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, and 10 mg/80 mg

Application Type/Number: NDA 200153

Applicant/Sponsor: Merck

OSE RCM #: 2012-2940

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

** This document contains proprietary data from the [REDACTED] (b) (4) [REDACTED] which cannot be shared outside of the FDA. Users wanting this information must contact a designated individual in the Division of Medication Error Prevention and Analysis who will gain approval from [REDACTED] (b) (4) [REDACTED].**

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Atozet, 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

The Applicant, Merck, initially submitted for review the proposed proprietary name request for Atozet on July 7, 2011 as part of the NDA. The proposed proprietary name, Atozet was found conditionally acceptable from a promotion and safety perspective by the Office of Prescription Drug Promotion (OPDP) and the Division of Medication Error Prevention and Analysis (DMEPA), respectively in OSE Review #2011-2469 dated September 26, 2011. On February 29, 2012, the application received a Complete Response (CR) Letter due to bioequivalence issues.

On December 14, 2012, Merck resubmitted the NDA and the request for review of the proposed proprietary name, Atozet to the NDA, and stated that none of the product characteristics has changed.

1.2 PRODUCT INFORMATION

The following product information is provided in the December 14, 2012 proprietary name submission.

- Indication: For reduction of cholesterol in primary hyperlipidemia and homozygous familial hypercholesterolemia.
- Route: Oral
- Dosage Form: Fixed-dose combination tablets
- Strengths: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg
- Dose and Frequency: One tablet by mouth once daily
- How Supplied: Physician Sample carton containing 3 pouches with each pouch containing 7 tablets; Trade Carton containing 9 pouches with each Trade Foil Pouch of 10 tablets
- Storage: Store at 20-25°C (68-77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]
- Container and Closure Systems: The drug product will be packaged in a vented (b) (4) blister with push-through aluminum lidding. The (b) (4) aluminum blister card is enclosed in a (b) (4) plastic case (for child resistance) which is contained in a (b) (4) aluminum pouch along with 2 oxygen scavengers and one (b) (4) desiccant canister.

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 Metabolism and Endocrinology Products 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

The January 11, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Atozet, is a coined term with no intrinsic meaning. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Seventy-eight practitioners participated in DMEPA's prescription studies. None of the 78 respondents in any of the simulation studies interpreted the name correctly. The most noteworthy misinterpretation occurred in the voice simulation study. In the voice study, one participant misinterpreted Atozet incorrectly as "Aricept," a drug product marketed for the treatment of Alzheimer's disease. This finding is noteworthy because it indicates that Atozet is vulnerable to name confusion with a marketed drug product and also because this misinterpretation represents a new finding. The previous simulation studies conducted for the completion of OSE Review #2011-2469 (dated September 26, 2011) did not include any misinterpretations of Atozet as Aricept. The significance of this finding will be discussed further in Section 3.

The other misinterpretations were misspellings of various portions of the name. Among the 30 inpatient responses, all 30 of the respondents misinterpreted the first letter 'A' as the letter 'S' (i.e. Atozet misinterpreted as "Stozet" n=25 "Stoyet" n=3 and "Stoget" n=2). Among the 25 participants in the voice simulation studies, 13 participants misinterpreted the letter 'o' for 'a' (i.e. AtOzet misinterpreted as "Atazet") and 10 participants misinterpreting the first letter 't' for 'd' (i.e. ATozet as "Adozet"). Lastly, in the outpatient simulation study, 22 participants misinterpreted the letter 'z' for 'r' (i.e. AtoZet as 'Atoret'). We have considered these misspelling variations in our look-alike and sound-alike searches. Appendix C provides a complete listing of interpretations from the verbal and written prescription studies. Aside from the

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, January 22, 2013 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 External Proprietary Name Risk Assessment

Given the recent findings of our name simulation studies indicating that Atozet is vulnerable to confusion with Aricept, DMEPA contacted Merck on February 5, 2013 to request submission of the external proprietary name risk assessment referenced in their letter dated December 14, 2012. This study was never submitted to DMEPA as part of the original Request for Proprietary Name Review submitted in 2011 or in the current request under consideration. No explanation on why the report was not submitted was provided. Hence, OSE Review #2011-2469 (dated September 26, 2011) did not evaluate or consider the findings in the overall risk assessment of the proposed name.

The external proprietary name risk assessment was conducted by (b) (4). The study report is dated March 4, 2011 and submitted on February 7, 2013. In the report, (b) (4) identified two notable look-alike and sound-alike names to Atozet: Azopt (look-alike) and Aricept (sound-alike). They describe Atozet as having “slight sound-alike similarity” with Aricept. The report also notes that Aricept is available as a 10 mg tablet, which “may be confused with the ezetimibe 10mg/atorvastatin 10mg strength of Atozet.” (b) (4) based this finding on the fact that the atorvastatin portion (e.g., 10 mg) of Atozet may be the only portion expressed on prescriptions or orders for Atozet since “the ezetimibe portion of the strength is the same for all of the Atozet dosage strength combinations.” (b) (4) further describes the risk of harm from such confusion as “moderate” due to the central nervous system and gastrointestinal effects associated with Aricept.

Atozet was also noted to have “slight look-alike similarity” to Azopt, a marketed drug formulated as a solution used for the treatment of open-angle glaucoma. The report notes a number of differences between Atozet and Azopt with regard to product characteristics, including that there are no overlapping strengths or units.

In the report, (b) (4) concluded that Atozet “may be able” to safely exist in the market for which it was tested.

(b) (4) analysis and conclusions were carefully considered in our overall risk assessment. Our analysis of the potential for confusion with Aricept is described in Section 3 Discussion and our analysis of the potential for confusion with Azopt is captured in Appendix E.

2.2.6 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, Atozet.

For this review, we searched for additional names of concern since the last review (see Table 1). Our analysis of the 20 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics.

Table 1: Collective List of Potentially Similar Names (DMEPA, Expert Panel Discussion (EPD), Other Disciplines, and External Name Study)					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Look Similar					
Alupent	EDP	Atapryl	EPD	Ala-tet	EPD
Alertab	EPD	Alert	EPD	Alacol	EPD
Alamast	EPD	Citrucel	EPD	Ala-Cort	EPD
Otozone	EPD	Atabex	EPD	Uloric	EPD
Ahist	EPD	Axert	EPD	Afrinol	EPD
Cromolyn	EPD	Atoca	EPD	Arogya (Pacha)	EPD
Azopt	EPD	Aricept	EPD		

Our analysis of the 20 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 19 of the 20 names will not pose a risk for confusion as described in Appendix D and E. However, based on our current analysis and the misinterpretation recorded in the voice simulation study, we find the name Atozet to be phonetically similar to Aricept, and thus vulnerable to confusion.

DMEPA had previously evaluated the proposed proprietary name, Atozet, and found the name conditionally acceptable (OSE Review#2011-2469 dated September 26, 2011).

However, during this evaluation of the name, one participant in the voice simulation study misinterpreted the name Atozet as “Aricept,” a drug currently marketed for the treatment of Alzheimer’s disease.

This finding is noteworthy for several reasons.

First, this finding indicates that Atozet is vulnerable to name confusion with a marketed drug product. A primary goal of our proprietary name evaluations is to avoid approving proprietary names that are prone to be confused and cause errors with other drug products. Although our simulation studies are not designed to provide conclusive evidence that a proposed name would not be confused with another drug product¹ given the small sample

¹ A simulation study designed to detect close to a zero percentage error rate with statistical significance would require an extremely large sample size (e.g. a sample of approximately 26,000 would be required to detect an error rate of 0.001 at the 0.05 significance level). This calculation was made to determine whether the error rate differs from 0.001 at a 0.05 significance level and 80% power, assuming the medication error rate of the sample is 0.0005. (published in FDA’s PDUFA Pilot Project Proprietary Name Review Concept Paper)

size employed (<100 participants generally), these studies can provide important qualitative data that can be used to identify the potential vulnerability of a proposed name to be misinterpreted when written or verbal orders are communicated. Thus, the misinterpretation of Atozet as another marketed drug product represents a fundamental safety concern for the proposed name under consideration.

Secondly, this finding is noteworthy because it is new. In the previous simulation studies, the misinterpretation of Atozet as “Aricept” did not occur. Several reasons could explain this. The simulation studies were performed using different handwriting and voice samples of the proposed name and the participants responding to the simulation studies differed. Both or either of these changes could explain differences in the qualitative findings of the simulation studies. Additionally, as previously described, name simulation studies are not designed to provide absolute assurance that a proposed name does not pose a risk of confusion given the small sample size used in these studies. Thus, a negative finding (i.e. no name confusion) from the previous series of prescription simulation studies does not supersede a positive finding of name confusion from this subsequent series of simulation studies. Conversely, a positive finding does supersede any previous findings since the simulation studies provide important insight to the vulnerability of a proposed name to be misinterpreted. Thus, this new information provides us with reason to revisit our previous Failure Modes and Effects Analysis of the Atozet and Aricept name pair conducted as part of OSE Review #2011-2469 dated September 26, 2011. That review determined that phonetic differences in the names would distinguish these names in verbal communications, and the misinterpretation in the voice simulation studies now provides reason to believe that this finding was incorrect.²

Based on the new findings, we carefully considered whether the phonetic similarity of Atozet would lead to error with Aricept given the phonetic similarity of the names and overlapping product characteristics.

With respect to the phonetic similarity of the names, we determined that the proposed proprietary name Atozet is phonetically similar to Aricept. Both names have 3 syllables with the stress placed on the first syllable. Within each syllable there are similarities as follows:

- First syllable: Although the *intended* pronunciation of the first vowel sound in both names differ (AT vs. Air; or /ə/ vs. /eɪ/), it is possible that both vowel sounds be pronounce as /ə/. The second sounds in both names are alveolar/post-alveolar. Therefore, the first syllables of both names are stressed, may begin with the same vowel sound /ə/ and end with an alveolar sound.
- Second syllable: The second syllable in both names are short weak syllables (oh vs. eh), that are influence by the sounds around them and may blend with either the previous and following sounds.

² OSE Review #2011-2469 concluded the following phonetic differences would prevent the names from being confused: the first syllable in Atozet ends with a “t” sound vs. “r” sound in Aricept and that the final syllable in Atozet does not have a “p” sound vs. Aricept has the sound “p”.

- Third syllable: The first sounds (/z/ vs. /s/) are affricative/fricative and alveolar, which may cause voicing assimilation and sound the same. The second sounds are the same (/ɛ/). The last sound (/t/ vs. /pt/) may sound the same as voice assimilation may occur between the /p/ and /t/ since both are plosive sounds. Therefore, the last syllables in both names may sound the same.

Since the names are vulnerable to confusion, we then analyzed the product characteristics to determine whether or not the name similarity would be likely to lead to errors in the usual practice setting. Both Aricept and Atozet are oral tablets that can be administered once daily. We note that Atozet has two ingredients, ezetimibe and atorvastatin, with the following strengths: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, and 10 mg/80 mg. Since the 10 mg of ezetimibe is common to all four strengths and the atorvastatin component varies across the four strengths, there is potential for this product to be prescribed in ordered referencing only the atorvastatin component (e.g. Atozet 10mg). Med-ERRS (a subsidiary for the Institute for Safe Medication Practices) published responses to a questionnaire posed to health care practitioners specifically related to the prescribing and dispensing of combination products³ and confirmed this practice does occur in the clinical setting. Aricept is a single ingredient product with the strengths 5 mg and 10 mg; thus, we find that there is a potential overlap of 10 mg between the two products if ordered as “Atozet 10 mg” or “Aricept 10 mg”. In this situation, an order for Atozet 10 mg daily could be misinterpreted as Aricept 10 mg daily by a pharmacist, nurse, or other practitioner who receives a verbal order or prescription thus resulting in a medication error.

In addition to being informed by the findings of the voice simulation studies in which Atozet was misinterpreted as Aricept, our FMEA is informed by our understanding of name confusion that has resulted in errors with other drug products. In this situation we considered post-marketing reports of confusion between combination drug products and single ingredient drug products that overlap in one of the strengths when strong orthographic or phonetic similarity exists. As an example, the products Janumet (Metformin and Sitagliptin) and Januvia (Sitagliptin) were confused with each other due to strong name similarity and overlap in one of the strengths⁴. Januvia is marketed in a 25 mg, 50 mg, and 100 mg tablet and Janumet is marketed in 500 mg/50 mg and 1000 mg/50 mg tablets. This may also occur because when prescribing combination drug products, the constant strength maybe dropped from the order (accidentally or purposely) and the medication that was interpreted on the order would still be dispensed without seeking clarification of the prescription. Moreover, even when there is not a direct overlap in strength, we have received post marketing reports of errors. (b) (4)

Another example includes confusion between

³ <http://www.med-errs.com/Question/Resulterr0408.asp>, accessed October 18, 2012

⁴ <http://www.ismp.org/newsletters/acutecare/articles/20080925-1.asp> accessed February 19, 2013.

(b) (4)

Janumet (Metformin and Sitagliptin) available in 500 mg/50 mg and 1000 mg/50 mg strengths and Jantoven (warfarin) available in strengths of 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, and 7.5 mg and 10 mg.

Collectively, our post-marketing experience with other drug products and the voice simulation study misinterpretation lead us to determine that the name Atozet is vulnerable to confusion with Aricept. Specifically, we have concern that practitioners may order Atozet 10mg/10mg as “Atozet 10 mg,” and that such verbal orders may be mistakenly interpreted as Aricept 10mg resulting in a medication error.

Our determination differs from the external proprietary name risk assessment was conducted by (b) (4) which concluded that Atozet “may be able” to safely exist in the market for which it was tested.

In the report, (b) (4) describes Atozet as having “slight sound-alike similarity” with Aricept. (b) (4) did not detail what attributes of the name they used to determine that this “sound-alike” similarity exists, nor do they describe how they determined this similarity to be “slight”. Notwithstanding, we find that the phonetic similarity of Atozet and Aricept to be concerning based on our phonetic analysis of the name and the misinterpretation recorded in our voice simulation study. We agree with (b) (4) that the 10 mg strength of Aricept “may be confused with the ezetimibe 10mg/atorvastatin 10mg strength of Atozet” based upon the fact that the atorvastatin portion (e.g., 10 mg) of Atozet may be the only portion expressed on prescriptions or orders. It is unclear why (b) (4) determined in the face of this potential confusion that the name Atozet “may be able” to safely exist in the market for which it was tested. Aricept is an actively marketed drug, and there conclusion appears at odds with their safety finding. Given this inconsistency, we are unable to explain why we disagree with (b) (4) position.

2.2.7 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products via e-mail on February 12, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Metabolism and Endocrinology Products on February 13, 2013, they stated no additional concerns with the proposed proprietary name, Atozet.

3 CONCLUSIONS

The proposed proprietary name is acceptable from a promotional perspective but not acceptable from a safety perspective. The proposed name is vulnerable to name confusion with Aricept. Therefore, the decision to deny the name will be communicated to the Applicant via letter (See *Section 4.1*).

If you have further questions or need clarifications, please contact Margarita Tossa, OSE project manager, at 301-796-4053.

(b) (4)

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Atozet, and have concluded that this name is unacceptable because Atozet is phonetically similar to the currently marketed product, Aricept (donepezil).

We acknowledge that this determination differs from our previous evaluation and conclusion communicated in the letter dated September 26, 2011. We further acknowledge that this determination differs from the external proprietary name risk assessment conducted by (b) (4) dated March 4, 2011 and submitted on February 7, 2013 that concludes that Atozet “may be able” to safely exist in the market for which it was tested.

The reason we have reached a different determination with respect to the safety of your proposed name is based upon the new safety information identified in the voice simulation studies, which was confirmed by our phonetic analysis of the Aricept/Atozet name pair. The details of our findings are described below.

In our current evaluation of your proposed name, one participant in the voice simulation study misinterpreted Atozet as Aricept. In our previous evaluation, the misinterpretation of Atozet as “Aricept” did not occur in the simulation studies that were conducted as part of that evaluation. Several reasons could explain why the misinterpretation did not occur in one simulation study versus another. The simulation studies were performed using different handwriting and voice samples of the proposed name and the participants responding to the simulation studies differed. Both or either of these changes could explain differences in the qualitative findings of the simulation studies. Additionally, name simulation studies are not designed to provide conclusive evidence that a proposed name does not pose a risk of confusion given the small sample size used in these studies. Thus, a negative finding (i.e. no name confusion) from the previous series of prescription simulation studies does not supersede a positive finding (i.e. name confusion) from this subsequent series of simulation studies. Conversely, a positive finding does supersede any previous findings since such a finding is an indication of the names vulnerability to confusion.

Thus, the new information garnered from the simulation studies caused us to revisit in this evaluation our previous Failure Modes and Effects Analysis of the Aricept/Atozet pair. Our previous conclusion that Atozet was conditionally acceptable was based on the fact that the name was not thought to present a risk for confusion with any marketed or pending drug or biologic names. Our FMEA did consider whether Atozet might be confused with Aricept, but at the time of that review we determined that phonetic differences in the names would distinguish these names in verbal communication. The evaluator in the safety review conducted for the letter dated September 26, 2011 letter concluded the following phonetic differences would prevent the names from being confused, Specifically, that reviewer asserted that the names were distinguishable when spoken because the first syllable in Atozet ends with a “t” sound versus the “r” sound in Aricept and the final syllable in Atozet does not have a “p” sound vs. Aricept has the sound “p”. However, the misinterpretation in the voice simulation studies conducted as part of this review now provides reason to conclude that this analysis and conclusion was incorrect.

With respect to the phonetic similarity of Atozet and Aricept, both names have 3 syllables with the stress placed on the first syllable. Within each syllable there are similarities as follows:

- First syllable: Although the *intended* pronunciation of the first vowel sound in both names differ (AT vs. Air; or /ə/ vs. /eɪ/), it is possible that both vowel sounds be pronounce as /ə/. The second sounds in both names are alveolar/post-alveolar. Therefore, the first syllables of both names are stressed, may begin with the same vowel sound /ə/ and end with an alveolar sound.
- Second syllable: The second syllable in both names are short weak syllables (oh vs. eh), that are influence by the sounds around them and may blend with either the previous and following sounds.
- Third syllable: The first sounds (/z/ vs. /s/) are affricative/fricative and alveolar, which may cause voicing assimilation and sound the same. The second sounds are the same (/ɛ/). The last sound (/t/ vs. /pt/) may sound the same as voice assimilation may occur between the /p/ and /t/ since both are plosive sounds. Therefore, the last syllables in both names may sound the same.

In addition to the phonetic similarity of Atozet and Aricept, we note that these products share a number of product characteristics that would lead errors in the usual practice setting. Both Aricept and Atozet are oral tablets that can be administered once daily. We note that Atozet has two ingredients, ezetimibe and atorvastatin, with the following strengths: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, and 10 mg/80 mg. Since the 10 mg of ezetimibe is common to all four strengths and the atorvastatin component varies across the four strengths, there is potential for this product to be prescribed and ordered referencing only the atorvastatin component (e.g. Atozet 10mg). Med-ERRS, a subsidiary for the Institute for Safe Medication Practices, published responses to a questionnaire posed to health care practitioners specifically related to the prescribing and dispensing of combination products⁷ and confirmed this practice does occur in the clinical setting. Aricept, which is a single ingredient product with the strengths 5 mg and 10 mg; thus, we find that there is a potential overlap of 10 mg between the two products if ordered as “Atozet 10 mg” or “Aricept 10 mg”. In this situation, an order for Atozet 10 mg daily could be misinterpreted as Aricept 10 mg daily by a pharmacist, nurse, or other practitioner who receives a verbal order or prescription thus resulting in a medication error. Our analysis is informed by our post-marketing surveillance of medication errors involving other drug products. Specifically, we are aware of post-marketing reports of errors that have occurred between combination drug products and single ingredient drug products that have similar names and overlapping or similar strengths.

Collectively, our post-marketing experience with other drug products and the voice simulation study misinterpretation lead us to conclude that the name Atozet is vulnerable to confusion with Aricept. Specifically, we have concern that practitioners may order Atozet 10mg/10mg as “Atozet 10 mg,” and that such verbal orders may be mistakenly interpreted as Aricept 10mg resulting in a medication error.

⁷ <http://www.med-errs.com/Question/Resulterr0408.asp>, accessed October 18, 2012

We further acknowledge that our determination also differs from the external proprietary name risk assessment conducted by (b) (4). This report was not submitted by you for consideration in our previous review, but was carefully evaluated as part of this review. (b) (4) concluded in their report that Atozet “may be able” to safely exist in the market for which it was tested.

In the report, (b) (4) describes Atozet as having “slight sound-alike similarity” with Aricept. (b) (4) did not detail what attributes of the name they used to determine that this “sound-alike” similarity exists, nor do they describe how they determined this similarity to be “slight”. Notwithstanding, we find that the phonetic similarity of Atozet and Aricept to be demonstrated by the misinterpretation recorded in our voice simulation study and our phonetic analysis of the name pair. We agree with (b) (4) that the 10 mg strength of Aricept “may be confused with the ezetimibe 10mg/atorvastatin 10mg strength of Atozet” based upon the fact that the atorvastatin portion (e.g., 10 mg) of Atozet may be the only portion expressed on prescriptions or orders. It is unclear why, in the face of this identified risk of name confusion, (b) (4) determined that the name Atozet “may be able” to safely exist in the market for which it was tested. Aricept is an actively marketed drug, and there conclusion appears at odds with their safety finding. Given this inconsistency, we are unable to explain why our conclusions differ with (b) (4) determination.

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.⁸

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

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

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

⁸ National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

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.⁹

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).

⁹ 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.¹⁰ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the

¹⁰ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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

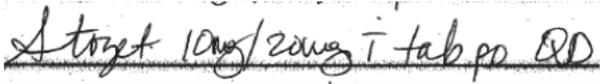
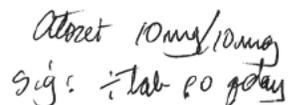
of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Atozet	Scripted May Appear as	Spoken May Be Interpreted as
'A'	FL, H, Ci, O, S, U	Any vowel
lowercase 'a'	el, ci, cl, d, o, u, c, e	Any vowel
lowercase 't'	r, f, x, l	d
lowercase 'o'	a, c, e, u	oh
lowercase 'z'	c, e, g, n, m, q, r, s, v, y	c, s, x
lowercase 'e'	a, l, l, o, u, p, c	i, y
lowercase 't'	r, f, x, l	d
Letter Strings		
'ze'	u	
'et'	d	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Atozet Study (Conducted on January 17, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Atozet 10 mg/10 mg One tab by mouth once daily</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

192 People Received Study

78 People Responded

Total	26	17	19	78	62
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL	
ADACEPT	0	1	0	1	
ADAZAC	0	1	0	1	
ADAZEC	0	1	0	1	
ADAZET	0	2	0	2	
ADECEPT	0	1	0	1	
ADISETS	0	1	0	1	
ADIVET	0	1	0	1	
ADIZET	0	2	0	2	
ARICEPT	0	1	0	1	
ATAVEX	0	1	0	1	
ATAZAC	0	2	0	2	
ATAZAT	0	1	0	1	
ATAZEPT	0	1	0	1	
ATAZET	0	3	0	3	
ATIVET	0	2	0	2	
ATIZEP	0	1	0	1	
ATIZEPT	0	1	0	1	
ATIZET	0	2	0	2	
ATORET	0	0	22	22	
ATORNET	0	0	1	1	

STOGET	2	0	0	2
STOYET	3	0	0	3
STOZET	25	0	0	25

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

Proprietary Name	Active Ingredient	Similarity to Atozet	Failure preventions
Alertab	Diphenhydramine HCl	<i>Look</i>	The pair have sufficient orthographic differences
	Cromolyn	<i>Look</i>	The pair have sufficient orthographic differences
Afrinol	Pseudoephedrine HCl	<i>Look</i>	The pair have sufficient orthographic differences
Arogya	Trichopus Zeylanicus	<i>Look</i>	The pair have sufficient orthographic differences
Atoca	Cranberry	<i>Look</i>	Name identified in Natural Medicine database. Unable to find product characteristics in commonly used drug databases.

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.

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Ala-tet (Tetracycline HCl)</p> <p>Dosage form and strength: Oral capsule: 250 mg</p> <p>Usual dose: 1 capsule 4 times per day, up to 2 gm (8 capsules) per day</p>	<p>Orthographic similarity: The beginning letter strings ‘Ato’ and ‘Ala’ appear orthographically similar when scripted. In addition, both names end with the letter string ‘et’</p> <p>Dosage form and Route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: The letter ‘z’ in position 4 may be scripted with a downstroke, further giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Ala-tet is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p> <p>Frequency: Atozet is prescribed as daily vs. Ala-tet is prescribed as 4 times daily.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Uloric (Febuxostat)</p> <p>Dosage form and strength: Oral tablet: 40 mg and 80 mg</p> <p>Usual dose: 1 tablet once daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Atoze’ and ‘Ulori’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral tablets</p> <p>Strength: Both Atozet and Uloric are available in multiple strengths. Although Atozet is a combination product, the Ezetimibe strength is constant thus may be considered a complete prescription when written with only the Atorvastatin strength (10 mg, 20 mg, 40 mg, and 80 mg). There is numerical overlap between the two strengths during prescription writing (<i>i.e.</i> 40 mg and 80 mg)</p> <p>Frequency: Both are prescribed as daily</p>	<p>Orthographic difference: The ending letter ‘t’ and ‘c’ appear orthographically different when scripted.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Atabex (Prenatal multivitamins and minerals with docusate, iron, and folic acid)</p> <p>Dosage form and strength: Oral tablets: Single strength</p> <p>Usual dose: 1 tablet daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Ato’ and ‘Ata’ and the ending letter strings ‘et’ and ‘ex’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral tablets</p> <p>Frequency: Both are prescribed as once daily</p>	<p>Orthographic difference: Atabex contains an upstroke ‘b’ in position 4 which is absent in Atozet. The letter ‘z’ in position 4 may be scripted with a downstroke, further giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Atabex is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Alupent (Metaproterenol Sulfate)</p> <p>Dosage form and strength: Oral tablet: 10 mg and 20 mg Oral Syrup: 10 mg/5 mL</p> <p>Usual dose: 20 mg (10 mL) 3 or 4 times per day.</p>	<p>Orthographic similarity: The beginning letter strings ‘Ato’ and ‘Alu’ appear orthographically similar when scripted and end with t</p> <p>Dosage form and Route of administration: Both are available as oral dosage forms</p> <p>Strength: Both Atozet and Alupent are available in multiple strengths. Although Atozet is a combination product, the Ezetimibe strength is constant thus may be considered a complete prescription when written with only the Atorvastatin strength (10 mg, 20 mg, 40 mg, and 80 mg). There is numerical overlap between the two strengths during prescription writing (<i>i.e.</i> 10 mg and 20 mg)</p>	<p>Orthographic difference: The letter strings ‘ze’ and ‘pen’ appear orthographically different when scripted. In addition, the ending letter strings ‘et’ and ‘ent’ appear orthographically different when scripted.</p> <p>Frequency: Atozet is prescribed as daily vs. Alupent is prescribed as three or four times daily</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Alamast (Pemirolast Potassium)</p> <p>Dosage form and strength: Ophthalmic solution: 0.1%</p> <p>Usual dose: 1 to 2 drops into affected eye(s) 4 times per day</p>	<p>Orthographic similarity: The beginning letter strings ‘Ato’ and ‘Ala’ appear orthographically similar when scripted and both end with letter ‘t’.</p>	<p>Orthographic difference: ze vs. mas</p> <p>Dosage form and Route of administration: Oral tablets vs. ophthalmic solution</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Alamast is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p> <p>Dose: 1 tablet vs. 1 to 2 drops Frequency: once daily vs. four times daily</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Otozone (Chloroxylonol, Hydrocortisone, and Pramoxine)</p> <p>Dosage form and strength: Otic solution: 0.1%-1%-1%</p> <p>Usual dose: Instill 3 to 5 drops to the affected ear(s) 3 to 4 times per day</p>	<p>Orthographic similarity: The beginning letter strings ‘Atoze’ and ‘Otozo’ appear orthographically similar when scripted.</p>	<p>Orthographic difference: The ending letter strings ‘t’ and ‘ne’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Otozone is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p> <p>Dose: 1 tablet vs. 3 to 5 drops</p> <p>Frequency: once daily vs. three to four times daily</p>
<p>Ahist (Chlorpheniramine Tannate)</p> <p>Dosage form and strength: Oral tablet: 12 mg</p> <p>Usual dose: 1 tablet every 12 hours</p>	<p>Orthographic similarity: Both begin with the letter ‘A’ and end with the letter ‘t’</p> <p>Dosage form and Route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: The letter strings ‘toze’ and ‘his’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Ahist is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Atapryl (Selegiline)</p> <p>Dosage form and strength: Oral tablet: 5 mg</p> <p>Usual dose: 1 tablet every 24 hours</p>	<p>Orthographic similarity: Both names begin with the letters ‘At’ and the letters ‘o’ and ‘a’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral tablets.</p>	<p>Orthographic difference: The ending letter strings ‘zet’ and ‘pryl’ appear orthographically different when scripted.</p> <p>Dosage form and Route of administration: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Atapryl is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p>
<p>Alert (Caffeine)</p> <p>Dosage form and strength: Oral tablets: 200 mg</p> <p>Usual dose: 1 tablet as needed; may repeat every 3 to 4 hours as needed. Do not exceed labeled dosage.</p>	<p>Orthographic similarity: The beginning letter strings ‘Atoz’ and ‘Aler’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral tablets.</p>	<p>Orthographic difference: The ending letter strings ‘ert’ and ‘zet’ appear orthographically different when scripted.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Axert (Almotriptan Maleate)</p> <p>Dosage form and strength: Oral tablet: 6.25 mg and 12.5 mg</p> <p>Usual dose: 6.25 mg to 12.5 mg, with the 12.5 mg dose tending to be a more effective dose in adults. If the headache is relieved after the initial almotriptan dose but returns, the dose may be repeated after 2 hours.</p>	<p>Orthographic similarity: The beginning letter strings ‘Atoz’ and ‘Axer’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral tablets</p>	<p>Orthographic difference: The ending letter strings ‘et’ and ‘t’ appear orthographically different when scripted.</p> <p>Strength: Both are available in multiple strengths and need to be specified for a complete prescription. There is no numerical overlap between strengths.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Alacol (Brompheniramine Maleate and Phenylephrine)</p> <p>Dosage form and strength: Oral drops: 0.4 mg-1 mg/mL Oral syrup: 2 mg-5 mg/5 mL</p> <p>Alacol DM (Brompheniramine Maleate; Dextromethorphan Hydrobromide; Phenylephrine HCl)</p> <p>Dosage form and strength: Oral drops: 1 mg-2 mg-0.4 mg/mL Oral syrup: 2 mg-10 mg-5 mg/5 mL</p> <p>Usual dose: Oral syrup: 10 mL every 4 hours, up to 60 mL per day</p>	<p>Orthographic similarity: The letters in ‘Atozet’ and ‘Alacol’ appear orthographically similar when scripted.</p>	<p>Strength: Both are available in multiple strengths and need to be specified for a complete prescription. There is no numerical overlap between strengths.</p> <p>Frequency: Atozet is prescribed as once daily vs. Alacol is prescribed every 4 hours.</p> <p>Dose: 1 tablet vs. xx mL</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Ala Cort (Hydrocortisone)</p> <p>Dosage form and strength: External cream: 1%</p> <p>Usual dose: Apply to the affected area as a thin film 2 to 4 times daily depending on the severity of the condition</p>	<p>Orthographic similarity: The beginning letter strings ‘Atoze’ and ‘Alaco’ appear orthographically similar when scripted. In addition, both names end with the letter ‘t’</p>	<p>Orthographic difference: The ending letter strings ‘et’ and ‘ort’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Ala Cort is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p> <p>Frequency: Atozet is prescribed as daily vs. Ala Cort is prescribed 2 to 4 times daily.</p> <p>Dose: 1 tablet vs. apply to affected area</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Staflex (Acetaminophen and Phenyltoloxamine citrate)</p> <p>Dosage form and strength: Fixed dose combination Oral tablet: 500 mg/55 mg</p> <p>Usual dose: 1 to 2 tablets every 6 hours</p>	<p>Orthographic similarity: The beginning letter strings ‘Ato’ and ‘Sta’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral tablets</p>	<p>Orthographic difference: The ending letter strings ‘zet’ and ‘flex’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Staflex is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p> <p>Frequency: Atozet is prescribed as daily vs. Stafles is prescribed every 6 hours</p>
<p>Stavzor (Valproic Acid)</p> <p>Dosage form and strength: Delayed-release oral capsules: 125 mg, 250 mg, 500 mg</p> <p>Usual dose: 10 to 15 mg/kg/day, up to 60 mg/kg/day. Average dose: 250 mg to 1250 mg by mouth per day, divided up to 3 times daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Atoz’ and ‘Stav’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: The ending letter strings ‘et’ and ‘zor’ appear orthographically different when scripted.</p> <p>Strength: Both are available in multiple strengths and need to be specified for a complete prescription. There is no numerical overlap between strengths.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Staxyn (Vardenafil HCl)</p> <p>Dosage form and strength: Oral dispersible tablet: 10 mg</p> <p>Usual dose: 1 tablet daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Ato’ and ‘Sta’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral tablets</p> <p>Strength: Although Atozet is available in multiple strengths and is required for a complete prescription and Staxyn is only available in single strengths and may be omitted, there is numerical overlap between the two strengths during prescription writing, if Staxyn strength is not omitted (<i>i.e. 10 mg</i>)</p> <p>Frequency: Both are prescribed as daily</p>	<p>Orthographic difference: The ending letter strings ‘zet’ and ‘xyn’ appear orthographically different when scripted.</p>

<p>Proposed name: <i>Atozet</i> (Ezetimibe and Atorvastatin)</p> <p>Dosage form and Strength(s): Fixed dose combination oral tablets: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg</p> <p>Usual dose: One tablet by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Adipex-P (Phentermine HCl)</p> <p>Dosage form and strength: Oral tablet and capsule: Single-strength 37.5 mg</p> <p>Usual dose: 1 capsule or tablet daily, administered before breakfast or 1 to 2 hours after breakfast</p>	<p>Orthographic similarity: Both names begin with the letter ‘A’ and the ending letter strings ‘et’ and ‘ex’ appear orthographically similar when scripted.</p> <p>Dosage form and Route of administration: Both are available as oral dosage forms</p> <p>Frequency: Both are prescribed as daily.</p>	<p>Orthographic difference: The letter strings ‘toz’ and ‘dip’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Adipex-P is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p>
<p>Azopt (Brinzolamide)</p> <p>Dosage form and strength: Ophthalmic suspension: 1%</p> <p>Usual dose: One drop in the affected eye(s) three times daily</p>	<p>Orthographic similarity: Both names begin with the letter ‘A’ and end with a cross stroke ‘t’</p> <p>Dose: One tablet vs. one drop</p>	<p>Orthographic difference: The letter string ‘ze’ and the letter ‘p’ appear orthographically different when scripted.</p> <p>Strength: Multiple vs. single. An order for Atozet will require strength as it is available in multiple strengths vs. Azopt is available in single strength and may be omitted. There is no overlap between the strength during prescription writing.</p>

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/s/

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

Proprietary Name Review

Date: September 26, 2011

Reviewer(s): Anne C. Tobenkin, PharmD.
Division of Medication Error Prevention and Analysis

Team Leader Lubna Merchant, PharmD, M.S.
Division of Medication Error Prevention and Analysis

Division Director Carol Holquist, R.Ph.
Division of Medication Error Prevention and Analysis

Drug Name: Atozet (Ezetimibe and Atorvastatin) Tablets

Strengths: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg

Application Type/Number: NDA 200153

Applicant/sponsor: Merck

OSE RCM #: 2011-2469

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Atozet, 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

The Applicant, Merck, submitted the proprietary name request for Atozet tablets on July 7, 2011 as part of the NDA. The name Atozet was not previously reviewed by DMEPA.

1.2 PRODUCT INFORMATION

Atozet is a fixed dose combination product which contains the currently marketed products, Zetia (Ezetimibe) and Lipitor (Atorvastatin). Atozet is indicated for reduction of cholesterol in primary hyperlipidemia and homozygous familial hypercholesterolemia. The proposed strengths of Atozet include: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg. The recommended dose is one tablet by mouth once daily. Atozet will be available unit of use consisting of 30 or 90 tablets (b) (4)

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolic and Endocrinology Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The August 22, 2011 United States Adopted Name (USAN) stem search identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The proposed name is composed of a single word, Atozet. Although not stated by the Applicant in the proprietary name submission, the proprietary name, Atozet, is derived from the two drug products (Atorvastatin and Zetia) contained in Atozet which is appropriate. The proposed name does not contain any components that can contribute to medication errors.

2.2.4 FDA Name Simulation Studies

Thirty Five practitioners participated in DMEPA's prescription studies. Common misinterpretations of the name include: 'S' for 'A', 'r' for 'z', and 'd' for 't'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies. One respondent in the Outpatient study misinterpreted the proposed name for the currently marketed product, Atrovent. This name was also identified during EPD and included in Appendix E. Additionally, multiple respondents in the voice study misinterpreted the name as variations of Ad-cept. Because this misinterpretation was similar to Aricept, this name was also included in Appendix E.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, July 18, 2011 e-mail, the Division of Metabolic and Endocrinology (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed name, Atozet. Table 1 on page 3 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Atozet identified by the primary reviewer, the Expert Panel Discussion (EPD), other review disciplines.

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

Look Similar		Look and Sound Similar		Sound Similar	
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Alocril	EPD	Adalat	EPD	Actoplus Met	EPD
Atacand	EPD	Atovex	EPD	Azilect	EPD
Cetralax	EPD	Abelcet	EPD	Adcetris***	SE
Atamet	EPD	(b) (4)	EPD	Apacet	EPD
Striant	EPD	Atozet	EPD	Aricept	SE
Otocort	EPD	Adacel	EPD		
Alavert	EPD	Axocet	EPD		
Adagen	EPD	Aldomet	EPD		
Azopt	EPD	Otozin	EPD		
(b) (4)	EPD	(b) (4)	EPD		
(b) (4)	EPD	Atamet	SE		
Aloprim	EPD	Ultracet	SE		
Cetacort	SE				
Antizol	EPD				
Atarax	EPD				
Ativan	EPD				
Stavzor	EPD				
Atripla	EPD				
Atrovent	EPD				
Sotret	EPD				
Fluocet	EPD				
Alophen	EPD				
Axotal	EPD				
Oforta	SE				
Actonel	EPD				
(b) (4)	EPD				

Look Similar		Look and Sound Similar		Sound Similar	
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Oxycet	EPD				

Our analysis of the 44 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics. We determined all 44 names will not pose a risk for confusion as described in Appendix D through E.

DMEPA communicated these findings to the Division of Metabolic and Endocrinology Products (DMEP) via e-mail on September 7, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DMEP on September 7, 2011, they stated no additional concerns with the proposed proprietary name, Atozet.

3 CONCLUSIONS

The proposed proprietary name, Atozet, is acceptable from both a promotional and safety perspective. However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

The proposed proprietary name, Atozet, 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.

If you have further questions or need clarifications, please contact Margarita Tossa, OSE project manager, at 301-796-4053.

3.1 COMMENTS TO THE APPLICANT

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

4 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

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

8. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)
USPTO provides information regarding patent and trademarks.
9. ***Clinical Pharmacology Online*** (www.clinicalpharmacology-ip.com)
Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.
10. ***Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at*** (www.thomson-thomson.com)
The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.
11. ***Natural Medicines Comprehensive Databases*** (www.naturaldatabase.com)
Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.
12. ***Access Medicine*** (www.accessmedicine.com)
Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.
13. ***USAN Stems*** (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)
USAN Stems List contains all the recognized USAN stems.
14. ***Red Book Pharmacy's Fundamental Reference***
Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.
15. ***Lexi-Comp*** (www.lexi.com)
Lexi-Comp is a web-based searchable version of the Drug Information Handbook.
16. ***Medical Abbreviations Book***
Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A

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

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

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

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

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the

¹ National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.² The product characteristics considered for this review appears in Appendix B1 of this review.

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

² 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 Division of Drug Marketing, Advertising, and Communications (DDMAC). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Simulation Studies

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

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

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

4. Comments from Other Review Disciplines

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

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.³ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

³ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Appendix B1 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

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

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

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

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

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

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

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

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

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the

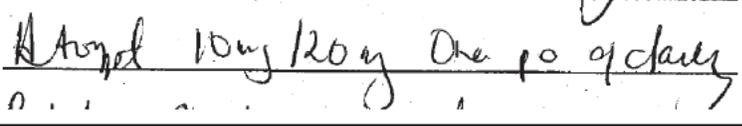
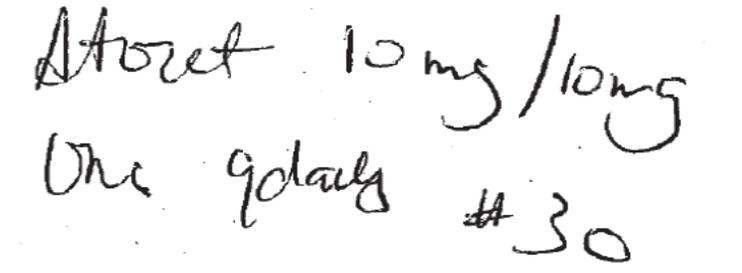
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Atozet	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'A'	U, O, Ci	"E"
lower case 't'	f, l, b	"d"
lower case 'o'	a, e, u	any vowel
lower case 'z'	g, m, y, j	"s", "c"
lower case 'e'	c, i, or l	any vowel
lower case 't'	f, l,	"d", "tte", "pt"

Appendix C: Prescription Simulation Samples and Results

Figure 1. Prescription Study (Conducted on 7/25/2011)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Atozet 10 mg/20 mg One po qdaily</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses.

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
ATROMET	ATORET	ADICEPT
ATOYZET	ATROVENT	ATIPEX
ATOMET	STORET	ATAZEPT
ATOZET	ATORET	ADACEPT
ATOZET	ATORET	ATISET
ATOZET	ATORET	ADADET
?	ATORET	ADAZEPT
ATOZET	ATORET	ADACET
ATOZEL	ATORET	ATTIZETTE
	ATOCET	ADIZET
	STORET	ADICEPT
	STORET	ADADEPT
	STORET	ADAZET

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

Atozet	(Ezetimibe and Atorvastatin)	Orthographic and Phonetic	Name evaluated in this review
(b) (4)			
Atovex	N/A	Orthographic and phonetic	Name only found in SAEGIS, not found in commonly used drug databases
Axotal	(Aspirin and Butalbital)	Orthographic	Product discontinued, no generic available
Apacet	(Acetaminophen)	Phonetic	Name only found in Micromedex, however did not include product characteristics

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.

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Alocril (Nedocromil)</p> <ul style="list-style-type: none"> - 2% ophthalmic solution, 5 mL - 1-2 drops in each eye twice daily 	<p>Orthographic Similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names have three upstrokes that are similarly situated - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Dose (one tablet vs. one drop) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has two cross-strokes vs. Alocril has no cross-strokes <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 2%, single strength, not required on prescription) - Route of administration (oral vs. ophthalmic) - Frequency of administration (once daily vs. twice daily) - Dosage form (tablet vs. solution)
<p>Atarax (Hydroxyzine)</p> <ul style="list-style-type: none"> - 10 mg, 25 mg, 50 mg, 100 mg oral tablets, - 100 mg/5 mL oral syrup - 40 mg to 400 mg by mouth in divided doses three to four times daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘At’ - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Strength overlap (10 mg) - Dosage form (tablet) - Route of administration (oral) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Atarax has two upstrokes <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Frequency of administration (once daily vs. three to four times daily as needed)
<p>Atacand (Candesartan)</p> <ul style="list-style-type: none"> - 4 mg, 8 mg, 16 mg, 32 mg oral tablets - 2 mg to 32 mg by mouth once or twice daily, maximum dose per day is 32 mg 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘At’ - Both names have three upstrokes - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Dose (one) - Dosage form (tablet) - Route of administration (oral) - Frequency of administration (once daily) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atazet has two cross-strokes vs. Atacand has one cross-stroke - Atazet appears shorter when scripted due to narrow letters such as ‘t’ and ‘e’ vs. Atacand <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 4 mg, 8 mg, 16 mg, 32 gm)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Ativan (Lorazepam)</p> <ul style="list-style-type: none"> - 0.5 mg, 1 mg, 2 mg oral tablets - 2 mg/mL, 4 mg/mL injection - 2 mg to 6 mg by mouth per day in two or three divided doses - 2 mg to 4 mg intravenous or intramuscular as needed 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘At’ - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Dose (one tablet) - Dosage form (tablet) - Route of administration (oral) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Ativan has two upstrokes <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 0.5 mg, 1 mg, 2 mg) - Frequency of administration (once daily vs. two to three times daily as needed)
<p>Cetralax (Ciprofloxacin)</p> <ul style="list-style-type: none"> - 0.2% otic solution, 0.25 mL single use containers, 14 per carton - One single use container instilled into the affected ear twice daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘At’ and ‘Cet’ appear similar when scripted - Both names have three upstrokes that are similarly situated - Both names are similar in length 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet ends with a cross-stroke vs. Cetralax does not end with a cross-stroke <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 0.2 %, single strength, not required on prescription) - Route of administration (oral vs. ear) - Frequency of administration (once daily vs. twice daily) - Dosage form (tablet vs. solution)
<p>Stavzor (Valproic acid)</p> <ul style="list-style-type: none"> - 125 mg, 250 mg, 500 mg oral capsules - starting dose is 750 mg by mouth daily in two or three divided doses, maximum recommended dosage is 60 mg/kg/day 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘St’ and ‘At’ can appear similar when scripted - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Route of administration (oral) - Dose (one) - Dosage form (oral solid; capsule, tablet) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Stavzor has two upstrokes - Atozet has two cross-strokes vs. Stavzor has one cross-stroke <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 125 mg, 250 mg, 500 mg) - Frequency of administration (once daily vs. two or three times daily)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Atamet (Carbidopa and Levodopa) Proprietary name is discontinued, however product still marketed</p> <ul style="list-style-type: none"> - 25 mg/100 mg, 25 mg/250 mg oral tablets - One to two tablets by mouth three to four times daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘At’ - Both names have three upstrokes that are similarly situated - Both names have two cross-strokes that are similarly situated <p>Product characteristics</p> <ul style="list-style-type: none"> - Route of administration (oral) - Dosage form (tablet) - Dose (one) 	<p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 25 mg/100 mg, 25 mg/250 mg) - Frequency of administration (once daily vs. three to four times daily) - Preliminary use data suggests that the name, Atamet, is no longer in use during prescribing/dispensing
<p>Atripla (Efavirenz, Emtricitabine, and Tenofovir)</p> <ul style="list-style-type: none"> - 600 mg/200 mg/300 mg oral tablet - One tablet by mouth once daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘At’ - Both names have three upstrokes that are similarly situated - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Route of administration (oral) - Frequency of administration (oral) - Dosage form (tablet) - Dose (one) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has a letter in between the downstroke (if ‘z’ is scripted) and upstroke vs. the downstroke and upstroke are next to one another in Atripla - Atozet ends with an upstroke vs. Atripla has a letter following the final upstroke - Atozet has two cross-strokes vs. Atripla has one cross-stroke <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 600 mg/200 mg/300 mg, single strength, not required on prescription)
<p>Atrovent (Ipratropium)</p> <ul style="list-style-type: none"> - 17 mcg per actuation, 200 actuations per canister - One to two inhalations four times a day, not to exceed 12 inhalations in 24 hours 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘At’ - Both names have three upstrokes that are similarly situated - Both names have two cross-strokes <p>Product characteristics</p> <ul style="list-style-type: none"> - Route of administration (oral) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has six letters vs. Atrovent has eight letters making it appear longer when scripted <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 17 mcg/actuation, single strength, not required on prescription) - Frequency of administration (once daily vs. four times daily) - Dosage form (tablet vs. inhaler)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Striant (Testosterone)</p> <ul style="list-style-type: none"> - 30 mg buccal system, 10 buccals per blister, 6 blisters per pack - One buccal to the gum region twice daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘St’ resembles ‘At’ when scripted - Both names have three upstrokes that are similarly situated - Both names have two cross-strokes that are similarly situated <p>Product characteristics</p> <ul style="list-style-type: none"> - Dosage form (solid oral; tablet, buccal) - Route of administration (oral) - Dose (one) 	<p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 30 mg, single strength, not required on prescription) - Frequency of administration (once daily vs. twice daily)
<p>Sotret (Isotretinoin)</p> <ul style="list-style-type: none"> - 10 mg, 20 mg, 30 mg, 40 mg oral capsule - 0.5 mg/kg to 2 mg/kg by mouth in two divided doses per day - 100 mg/m² by mouth once daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both name have three upstrokes - Both names have two cross-strokes - both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Strength (10 mg, 20 mg, 40 mg) - Route of administration (oral) - Frequency of administration (once daily) - Dosage form (oral solid: tablet, capsule) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atrozet has the first two upstrokes next to one another vs. Sotret has a letter in between the first two upstrokes <p>Product characteristic differences</p> <ul style="list-style-type: none"> - The prescribed dose for Sotret that is once daily will exceed that maximum recommend dose of Atrozet
<p>Otocort (Hydrocortisone, Neomycin, and Polymixin) Proprietary name discontinued, however product still marketed</p> <ul style="list-style-type: none"> - 1 mg /3.5 mg/ 10,000 Units/mL otic solution, otic suspension - Three to four drops in each ear three to four times daily for 10 days 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘Ato’ resembles ‘Oto’ when scripted - Both names have three upstrokes that are similarly situated - Both names have two cross-strokes that are similarly situated 	<p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 1/3.5 mg/10,000 Units/mL, single strength, not required on prescription) - Frequency of administration (once daily vs. three to four times daily) - Route of administration (oral vs. ear) - Dosage form (tablet vs. solution) - Dose (one vs. three to four drops) - Preliminary use data suggests that, Otocort, is not utilized during prescribing/dispensing

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Fluocet (Fluocinolone) Proprietary name discontinued, however product still marketed</p> <ul style="list-style-type: none"> - 0.025% topical cream - Apply sparingly to affected area two to four times daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘At’ can appear similar to ‘Fl’ when scripted - Both names have three upstrokes - Both names end with a cross-stroke 	<p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 0.025%, single strength, not required on prescription) - Frequency of administration (once daily vs. two to four times daily) - Route of administration (oral vs. topical) - Dosage form (tablet vs. cream) - Dose (one vs. sparingly) - Preliminary use data suggests that the name, Otocort, is no longer in use during prescribing/dispensing
<p>Alavert (Loratadine) OTC</p> <ul style="list-style-type: none"> - 10 mg oral tablet - One tablet by mouth once daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘Ato’ resembles ‘Ala’ when scripted - Both names have three upstrokes that are similarly situated - Both names ends with a cross-stroke - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Frequency of administration (once daily) - Route of administration (oral) - Dosage form (tablet) - Dose (one) 	<p>Orthographic differences:</p> <ul style="list-style-type: none"> - Atozet has two cross-strokes vs. Alavert has one cross-stroke - Atozet has one letter in between the ‘z’ and ‘t’ vs. Alavert has two letters between the ‘v’ and ‘t’ making it appear longer when scripted <p>Product characteristic differences:</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 10 mg, single strength, not required on prescription, additionally, ‘10 mg’ strength designation would be considered an incomplete prescription order for Atozet and would be questioned by a health care practitioner)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Alophen (Bisacodyl)</p> <ul style="list-style-type: none"> - 5 mg oral tablet - 5 mg to 30 mg by mouth per day 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘At’ resembles ‘Al’ when scripted - Both names have three upstrokes <p>Product characteristics</p> <ul style="list-style-type: none"> - Obtainable strength (10 mg) - Dosage form (tablet) - Route of administration (oral) - Frequency of administration (once) - Dose (one) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has two cross-strokes vs. Alophen has no cross-strokes - Atozet has a letter in between the downstroke (is ‘z’ is scripted) and final upstroke vs. Alophen has a downstroke next to the final upstroke - Atozet ends with an upstroke vs. Alophen has two letters after the final upstroke
<p>Adagen (Pegademase bovine)</p> <ul style="list-style-type: none"> - 250 Units/mL, 1.5 mL vial - titration from 10 units/kg, 15 units/kg, 20 units/kg, 25 units/kg, 30 units/kg intramuscularly per week 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names are similar in length - Both names have similarly situated downstrokes (if ‘z’ is scripted) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has two corss-strokes vs. Adagen has no cross-strokes - Atozet has three upstrokes vs. Adagen has two upstrokes <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Dose (one tablet vs. units/kg, weight based) - Route of administration (oral vs. intramuscular) - Frequency of administration (once daily vs. once weekly) - Dosage form (tablet vs. solution)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Azopt (Brinzolamide)</p> <ul style="list-style-type: none"> - 1% ophthalmic suspension, 5 mL, 10 mL, 15 mL - One drop in the affected eye(s) three times daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names ends with an upstroke and cross-stroke <p>Product characteristics</p> <p>Dose (one tablet vs. one drop)</p>	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Azopt has two upstrokes - Atozet has a letter in between the downstroke (if ‘z’ is scripted) and the upstroke vs. Azopt has the downstroke next to the upstroke <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 1%, single strength, not required on prescription) - Route of administration (oral vs. ophthalmic) - Frequency of administration (once daily vs. three times daily) - Dosage form (tablet vs. solution)
<p>Actonel (Risedronate)</p> <ul style="list-style-type: none"> - 5 mg, 35 mg (pack of 4), 150 mg oral tablet (pack of 1) - 5 mg by mouth once daily, 35 mg by mouth once weekly, 150 mg by mouth once a month 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names have three upstrokes - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Frequency of administration (once daily) - Dosage form (tablet) - Dose (one) - Obtainable strength (10 mg) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has the first two upstrokes next to one another vs. Actonel has a letter in between the first two upstrokes - Atozet has two cross-strokes vs. Actonel has one cross-stroke <p>Product characteristic differences</p> <ul style="list-style-type: none"> - 10 mg strength once daily exceeds that recommended dose of once daily administration of Actonel
<p>Oxycet (Acetaminophen and Oxycodone)</p> <ul style="list-style-type: none"> - 325 mg/5 mg oral tablet - One to two tablets by mouth every 4 to 6 hours as needed 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘A’ and ‘O’ appear similar when scripted - Both names ends with an upstroke/cross-stroke - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Dose (one) - Route of administration (oral) - Dosage form (tablet) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Oxycet has two upstrokes <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 325 mg/5 mg, single strength, not required on prescription) - Frequency of administration (once daily vs. every 4 to 6 hours, as needed)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Aloprim (Allopurinol)</p> <ul style="list-style-type: none"> - 500 mg per vial - 200 mg to 400 mg/m² intravenous infusion as a single infusion once daily or in equally divided infusions every 6, 8 or 12 hours 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘At’ and ‘Al’ appear similar when scripted - Both names are similar in length - Both names have a downstroke in the middle of the name (if ‘z’ is scripted) <p>Product characteristics</p> <ul style="list-style-type: none"> - Frequency of administration (once daily) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Aloprim has two upstrokes - Atozet has two cross-strokes vs. Aloprim has no cross-strokes - Atozet ends with an upstroke vs. Aloprim does not end with an upstroke <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Dose (one tablet vs. 200 mg/m² to 400 mg/m², weight based regimen) - Route of administration (oral vs. intravenous) - Dosage form (tablet vs. powder for infusion)
<p>Antizol (Fomepizole)</p> <ul style="list-style-type: none"> - 1.5 g (1 g/mL) - Loading dose of 20 mg/kg followed by 10 mg/kg or 15 mg/kg intravenous infusion every 12 hours until ethylene glycol is undetectable 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names have three upstrokes - Both names end with an upstroke - Both names are similar in length 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has the first two upstrokes next to one another vs. Antizol has a letter in between the first two upstrokes - Atozet has two cross-strokes vs. Antizol has one cross-stroke <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Dose (one tablet vs. 10 mg/kg to 20 mg/kg, weight based dosing) - Route of administration (oral vs. intravenous) - Frequency of administration (once daily vs. twice daily until levels are undetectable) - Dosage form (tablet vs. solution)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Adacel (Tetanus, Diphtheria, Pertussis, [Tdap])</p> <ul style="list-style-type: none"> - 1 dose per vial (0.5 mL) - 0.5 mL intramuscularly once in clinic 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names have three upstrokes - Both names are similar in length <p>Phonetic Similarity</p> <ul style="list-style-type: none"> - “At” sounds similar to “Ad” - Both names have three syllables 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has two cross-strokes vs. Adacel has no cross-strokes <p>Phonetic differences</p> <ul style="list-style-type: none"> - Atozet ends with a “t” sound vs. Adacel ends with an “l” sound <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Dose (one tablet vs. 0.5 mL) - Route of administration (oral vs. intramuscular) - Frequency of administration (once daily vs. once while in clinic) - Dosage form (table vs. solution)
<p>Axocet (Butalbital and Acetaminophen) Proprietary name discontinued, product still marketed</p> <ul style="list-style-type: none"> - 50 mg/650 mg oral capsule - one capsule every 6 hours as needed, not to exceed 6 capsules a day 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names end with an upstroke/cross-stroke - Both names are similar in length <p>Product characteristics</p> <ul style="list-style-type: none"> - Dosage form (tablet) - Route of administration (oral) - Dose (one) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Axocet <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 50 mg/650 mg, single strength, not required on prescription) - Preliminary use data suggests that the name, Axocet, is no longer in use during prescribing/dispensing

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Adalat (Nifedipine)</p> <ul style="list-style-type: none"> - 30 mg, 60 mg, 90 mg oral tablets - One tablet by mouth once daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names end with an upstroke/cross-stroke - Both names are similar in length <p>Phonetic Similarity</p> <ul style="list-style-type: none"> - “At” and “Ad” sound similar - Both names are 3 syllables - Both end with a “t” sound <p>Product characteristics</p> <ul style="list-style-type: none"> - Route of administration (oral) - Dosage form (tablet) - Dose (one) - Obtainable strength (30 mg) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet three upstrokes vs. Adalat has four upstrokes - Atozet has two cross-strokes vs. Adalat has one cross-stroke <p>Phonetic differences</p> <ul style="list-style-type: none"> - The third syllable in Atozet starts with a “z” sound vs. the third syllable starts with the sound “l” in Adalat <p>Product characteristic differences</p> <ul style="list-style-type: none"> - The 30 mg dose can only be achieved by exceeding the maximum dose of 10 mg per day of ezetimibe
<p>Aldomet (Methyldopa)</p> <p>Proprietary name discontinued</p> <ul style="list-style-type: none"> - 125 mg, 250 mg, 500 mg oral tablet - 500 mg to 2000 mg by mouth taken two to four times daily in divided doses 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘At’ and ‘Al’ appear similar when scripted - Both names end with an upstroke/cross-stroke - Both names are similar in length <p>Phonetic</p> <ul style="list-style-type: none"> - Both names begin with the sound “A” - Both names are three syllable - Both names end with the sound “t” <p>Product characteristics</p> <ul style="list-style-type: none"> - Dosage form (tablet) - Route of administration (oral) - Dose (one) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Aldomet has four upstrokes - Atozet has two cross-strokes vs. Aldomet has one cross-stroke <p>Phonetic differences</p> <ul style="list-style-type: none"> - The first syllable in does not contain an “l” sound in Atozet vs. the first syllable in Aldomet contains the sound “l” - The last syllable in Atozet starts with the sound “z” vs. the last syllable starts with the sound “m” in Aldomet <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 125 mg, 250 mg, 500 mg) - Frequency of administration (once daily vs. two to four times daily)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Otozin (Antipyrine, Benzocaine, Zinc acetate)</p> <ul style="list-style-type: none"> - 5.4%/1%/1% otic solution - Instill into the ear three times daily for 2 to 3 days 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘At’ and ‘Ot’ appear similar when scripted - Both names have ‘z’ in the middle - Both names are similar in length <p>Phonetic similarity</p> <ul style="list-style-type: none"> - Both names have three syllables - Both name have a “t” sound at the end of the first syllable 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Otozin has two upstrokes - Atozet has two cross-stroke vs. Otozin has one <p>Phonetic</p> <ul style="list-style-type: none"> - Atozet ends with the sound “t” vs. Otozin ends with the sound “n” <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 5.4%/1%/1%, single strength, not required on a prescription) - Route of administration (oral vs. ear) - Frequency of administration (once daily vs. three times daily) - Dosage form (tablet vs. solution)
<p>Abelcet (Amphotericin B)</p> <ul style="list-style-type: none"> - 100 mg/20 mL injection suspension - 5 mg/kg intravenous infusion once daily 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names end with an upstroke/cross-stroke - Both names are similar in length <p>Phonetic similarity</p> <ul style="list-style-type: none"> - Both names begin with the sound “A” - Both names have three syllables - Both names end with the sound “t” <p>Product characteristics</p> <ul style="list-style-type: none"> - Frequency of administration (once daily) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet has three upstrokes vs. Abelcet has four upstrokes - Atozet has two cross-strokes vs. Abelcet has once cross-stroke <p>Phonetic differences</p> <ul style="list-style-type: none"> - The first syllable in Atozet has the sound “t” vs. the first syllable has the sound “b” - The second syllable in Atozet has the sound “o” vs. “el” in Abelcet <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Dose (one tablet vs. 5 mg/kg, weight based dosing) - Route of administration (oral vs. intravenous) - Dosage form (tablet vs. suspension)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Azilect (Rasagiline)</p> <ul style="list-style-type: none"> - 0.5 mg, 1 mg oral tablet - One tablet by mouth once daily 	<p>Phonetic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ - Both names have three syllables - Both names ends with the sound “t” - Both names a “z” sound <p>Product characteristics</p> <ul style="list-style-type: none"> - Frequency of administration (once daily) - Route of administration (oral) - Dosage form (oral) 	<p>Phonetic differences</p> <ul style="list-style-type: none"> - The first syllable sound in Atozet ends with the “t” sound vs. the first syllable sound in Azilect ends with the “z” sound - The last syllable in Atozet starts with the sound “z” vs. “l” in Azilect - The last syllable in Atozet does no have the sound “c” vs. Azilect has the sound “c” in the last syllable <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 0.5 mg, 1 mg)
<p>Actoplus Met (Pioglitazone and Metformin)</p> <ul style="list-style-type: none"> - 15 mg/500 mg, 15 mg/850 mg oral tablets - One tablet once or twice daily 	<p>Phonetic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘A’ <p>Product characteristics</p> <ul style="list-style-type: none"> - Frequency of administration (once daily) - Dosage form (tablet) - Dose (one) - Route of Administration (oral) 	<p>Phonetic differences</p> <ul style="list-style-type: none"> - Atozet is three syllables vs. Actoplus Met is four syllable - The first syllable in Atozet does not have a “c” sound vs. Actoplus Met has a “c” sound - The third syllable in Atozet has the “zet” vs. the third syllable has the sound “plus” in Actoplus Met <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 15 mg/500 mg, 15 mg/850 mg)

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Ultracet (Tramadol and Acetaminophen)</p> <p>- 37.5 mg/325 mg oral tablets</p> <p>- One to two tablets by mouth every 4 to 6 hours, not to exceed 8 tablets a day</p>	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘A’ and ‘U’ appear similar when scripted - Both names have two cross-strokes that are similarly situated <p>Phonetic similarity</p> <ul style="list-style-type: none"> - Both names are three syllables - Both names end with the sound “set” <p>Product characteristics</p> <ul style="list-style-type: none"> - Dosage form (tablet) - Route of administration (oral) - Dose (one) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet is six letters vs. Ultracet is eight letters making it appear longer when scripted - Atozet has three upstrokes vs. Ultracet has four upstrokes <p>Phonetic differences</p> <ul style="list-style-type: none"> - Atozet does not have an “l” sound in the first syllable vs. Ultracet has an “l” sound in the first syllable <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 37.5 mg/325 mg, single strength, not required on prescription) - Frequency of administration (once daily vs. every 4 to 6 hours)
<p>Adcetris*** (Bretuximab) IND (b) (4)</p> <p>- 50 mg per vial</p> <p>- 1.8 mg/kg infused over 30 minutes once every 3 weeks</p>	<p>Phonetic similarity</p> <ul style="list-style-type: none"> - “At” and “Ad” sound similar when spoken - Both names have three syllables 	<p>Phonetic differences</p> <ul style="list-style-type: none"> - The middle syllable in Atozet emphasizes the “o” sound vs. “et” in Adcetris - Atozet ends with the sound “et” vs. Adcetris ends with the sound “ris” <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Dose (one vs. 1.8 mg/kg, weight based regimen) - Route of administration (oral vs. intravenous) - Frequency of administration (once daily vs. once every 3 weeks) - Dosage form (tablet vs. powder for infusion)
<p>Cetacort (Hydrocortisone) Proprietary name discontinued, product still marketed</p> <p>- 0.25%, 0.5%, 1% topical lotion</p> <p>- Apply sparingly to affected areas two to four times daily</p>	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘A’ and ‘Ce’ appear similar when scripted - Both names have three upstrokes - Both names have two cross-strokes that are similarly situated 	<p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 0.25%, 0.5%, 1%) - Route of administration (oral vs. topical) - Frequency of administration (once vs. two to four times per day) - Dosage form (tablet vs. lotion) - Dose (one vs. sparingly) - Preliminary use data suggests this name is no longer used during prescribing/dispensing

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Oforta (Fludarabine)</p> <ul style="list-style-type: none"> - 10 mg oral tablets - 40 mg/m² (30 mg to 100 mg) by mouth once daily for 5 consecutive days 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - ‘At’ and ‘Of’ appear similar when scripted - Both names have three upstrokes - Both names have two cross-strokes <p>Product characteristics</p> <ul style="list-style-type: none"> - Strength overlap (10 mg) - Dosage form (tablet) - Route of administration (oral) - Frequency of administration (once daily) 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Atozet ends with an upstroke/cross-stroke vs. Oforta has a letter following the final upstroke/cross-stroke - Atozet has three letters in between the final two upstrokes vs. Oforta has two letters between the final two upstrokes <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Dose (one tablet vs. multiple tablets)
<p>Atamet (Carbidopa and Levodopa) Proprietary name discontinued, product still marketed</p> <ul style="list-style-type: none"> - 25 mg/100 mg, 25 mg/250 mg oral tablets - One tablet by mouth four times daily (maximum dose is per day 8 tablets of 25 mg/250 mg) 	<p>Orthographic similarity</p> <ul style="list-style-type: none"> - Both names begin with ‘At’ - Both names have three upstrokes - Both names have two cross-strokes that are similarly situated - Both names are similar in length <p>Phonetic</p> <ul style="list-style-type: none"> - Both names begin with the sound “At” - Both names have three syllables - Both names end with the sound “et” <p>Product characteristics</p> <ul style="list-style-type: none"> - Route of administration (oral) - Dosage form (tablet) - Dose (one) 	<p>Phonetic differences</p> <ul style="list-style-type: none"> - The final syllable in Atozet begins with the sound “z” vs. the final syllable starts with the sound “m” in Atamet <p>Product characteristic differences</p> <ul style="list-style-type: none"> - Strength (10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg vs. 25 mg/100 mg, 25 mg/250 mg) - Frequency of administration (once daily vs. two to four times daily) - Preliminary use data suggests this name is no longer utilized during prescribing/dispensing

<p>Proposed name (s): Atozet (Ezetimibe and Atorvastatin)</p> <p>Strengths and dosage form: 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg oral tablets</p> <p>Usual Dose: One tablet by mouth once daily</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</p>
<p>Aricept (Donepezil)</p> <ul style="list-style-type: none"> - 5 mg, 10 mg oral tablet - 1 mg/mL oral solution - One tablet or 5 mL or 10 mL by mouth once daily 	<p>Phonetic similarity</p> <ul style="list-style-type: none"> - Both names begin with “A” - Both names are three syllables - Both names end with a “t” sound <p>- Product similarities</p> <ul style="list-style-type: none"> - Strength (10 mg) - Route of administration (oral) - Dosage form (tablet) - Frequency of administration (once daily) 	<p>Phonetic differences</p> <ul style="list-style-type: none"> - The first syllable in Atozet ends with a “t” sound vs. “r” sound in Aricept - The final syllable in Atozet does not have a “p” sound vs. Aricept has the sound “p”

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/s/

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