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APPLICATION NUMBER:

22-222Orig1s000

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: December 6, 2011

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Drug Name and strength(s): Ultrasa (Pancrelipase) Delayed-release Capsules
13,800 USP units Lipase;
27,600 USP units Amylase;
27,600 USP units Protease
and
20,700 USP units Lipase;
41,400 USP units Amylase;
41,400 USP units Protease
and
23,000 USP units Lipase;
46,000 USP units Amylase;
46,000 USP units Protease

Application Type/Number: NDA 022222

Applicant: Axcan Pharma

OSE RCM #: 2011-3388

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

CONTENTS

1	INTRODUCTION	1
1.1	Regulatory History	1
1.2	Product Information	1
2	RESULTS	2
2.1	Promotional Assessment	2
2.2	Safety Assessment.....	2
3	CONCLUSIONS.....	5
4	REFERENCES.....	6
	APPENDICES.....	8

1 INTRODUCTION

This review evaluates the proposed proprietary name, Ultresa, 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

Ultrase MT12, Ultrase MT18 and Ultrase MT20 have been marketed without an approved NDA since October, 1991. In response to the ‘Guidance for Industry: Exocrine Pancreatic Insufficiency Drug Products-Submitting NDAs’ dated April, 2006, the Applicant has submitted an NDA for approval. The Agency regulatory history of this product is as follows:

- May 30, 2008- DMEPA evaluated the name, Ultrase MT previously (OSE #2007-1913) and found the name vulnerable to confusion with the trademarked name, Altace and the parent drug Ultrase in addition to containing letter and numeric suffixes that could lead to medication errors. Furthermore, we objected to the name because it contained the United States Adopted Names (USAN) stem, ‘-ase’.
- March 12, 2009- the Applicant submitted three new names (Ultrase MT 13,800, Ultrase MT 20,700 and Ultrase MT 23,000) and three alternative names (Ultrase 13,800, Ultrase 20,700 and Ultrase 23,000). DMEPA objected to the use of these names (correspondence dated June 10, 2009) due to the inclusion of a USAN stem in the proprietary name and unacceptable modifiers.

Ultresa (Pancrelipase) Delayed-release Capsules (NDA 022222) is the subject of a Class-II resubmission dated September 1, 2011. On November 28, 2010, the agency issued a Complete Response letter for this Application due to deficiencies identified. DMEPA previously reviewed the proposed proprietary name, Ultresa in OSE Review #2009-1286, dated October 2, 2009, and found the name conditionally acceptable. As part of the review of the re-submission, the Applicant submitted a new request for the review of the proposed proprietary name, Ultresa on September 29, 2011.

1.2 PRODUCT INFORMATION

Ultresa (Pancrelipase) Capsules is a combination of porcine-derived Lipases, Proteases, and Amylases indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions. Ultresa is not interchangeable with other pancrelipase products. Ultresa is dosed by Lipase units, and is individualized and determined by the degree of steatorrhea present and the fat content of the diet. Therapy should begin with 500 lipase units/kg/meal (children 4 years and older and weight 28 kg or greater and adults) to 1000 Lipase units/kg/meal (children older than 12 months and younger than 4 years and weight 14 kg or greater) to a maximum of 2,500 Lipase units/kg/meal (or less than or equal to 10,000 Lipase units/kg/day), or less than 4,000 Lipase units/gram fat ingested/day. For children or patients unable to swallow intact capsules, the contents may be sprinkled on applesauce, yogurt, and other acidic food with pH 4.5 or less.

Ultresa will be available in the following three formulations in bottles of 100 and 500 (only the 23,000 USP units Lipase):

- 1) 13,800 USP units of Lipase, 27,600 USP units of Amylase and 27,600 USP units of Protease;
- 2) 20,700 USP units of Lipase; 41,400 USP units of Amylase and 41,400 USP units of Protease;
- 3) 23,000 USP units of Lipase, 46,000 USP units of Amylase and 46,000 USP units of Protease.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Gastroenterology and Inborn Error Products concurred with the findings of OPDP'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 United States Adopted Name (USAN) stem search conducted on October 13, 2010, 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 a single word that does not contain any components (i.e., modifier, dosage form, frequency, indications, etc.) that is misleading or can contribute to medication error. Additionally, the Applicant states that the proposed proprietary name, Ultresa, utilizes a blank canvas prefix combined with a suffix that subtly suggests triple enzyme.

2.2.3 FDA Name Simulation Studies

Twenty-three practitioners responded to DMEPA's prescription studies. None of responses overlapped with other drug names. Sixteen participants interpreted the proposed proprietary name correctly as 'Ultresa' with eight correct interpretations (n=8) occurring with inpatient orders, and eight correct interpretations (n=8) occurring with outpatient orders. The remaining seven participants misinterpreted the name, Ultresa. The most common misinterpretation occurred with four voice order participants misinterpreting the letter 'U' as the letter 'A' and five participants including an additional letter 's' in the name. One participant in the inpatient prescription studies misinterpreted the letter 's' as the letter 'x'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 External Proprietary Name Risk Assessment

The Applicant submitted an external evaluation of the proposed proprietary name risk assessment conducted by the (b) (4) ((b) (4) on July 7, 2009, as part of the original submission of the Application. A total of twelve names were identified and evaluated by (b) (4) Those names were also evaluated by the safety evaluator in OSE Review #2009-1286, dated October 2, 2010. The Applicant did not submit an external evaluation of the proposed proprietary name in the September 28, 2011 submission; however, we will re-evaluate the 12 names, previously evaluated in the October 2, 2010 review for accuracy.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, October 13, 2011 e-mail, the Division of Gastroenterology and Inborn Errors Products (DGIEP) 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

Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Ultresa (see Appendix B). These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also included the names identified by (b) (4) that were not previously identified by DMEPA and require further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, (b) (4) and Other Disciplines)

Look Similar		Sound Similar		Look and Sound Similar	
Name	Source	Name	Source	Name	Source
Ultrasex	EPD Panel	Atreza	Safety Evaluator and (b) (4)	Ultracet	EPD Panel and (b) (4)
UltraAC	EPD Panel	Elestrin	Safety Evaluator	Ultrase	EPD Panel and (b) (4) (see regulatory history)
Ultane	EPD Panel			Ultrase MT	EPD Panel (see regulatory history)
Ultram	EPD Panel and (b) (4)			Ultiva	EPD Panel and (b) (4)

Table 1: Continued

Look Similar		Sound Similar		Look and Sound Similar	
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Altace	EPD Panel and (b) (4)			(b) (4)	EPD Panel
Ultrane	EPD Panel			Ultrasul	EPD Panel
Ulticer	EPD Panel			(b) (4)	EPD Panel
Valtrex	EPD Panel			(b) (4)	EPD Panel
Voltaren	EPD Panel			Ultracef	EPD Panel
Ultravate	EPD Panel			(b) (4)	Safety Evaluator
Ultravist	EPD Panel				
Ultrax	EPD Panel				
Ultratag	EPD Panel				
Ultreon	EPD Panel				
Altrevin	EPD Panel				
Valturna	EPD Panel				
Uloric	EPD Panel				
Alesse	(b) (4)				
Isentress	(b) (4)				
Trinessa	(b) (4)				
Ultima	(b) (4)				
Ultram ER	(b) (4)				
Verdeso	(b) (4)				
Afresa	Safety Evaluator				
Abreva	Safety Evaluator				
(b) (4)	Safety Evaluator				
(b) (4)	Safety Evaluator				

Table 1: Continued

Look Similar		Sound Similar		Look and Sound Similar	
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Actiza	Safety Evaluator				
(b) (4)	Safety Evaluator				
Vitraxe	Safety Evaluator				
(b) (4)	Safety Evaluator				
Ultracal	Safety Evaluator				
Altavera	Safety Evaluator				
Ultrason	Safety Evaluator				
Ultair	Safety Evaluator				
Altraco	Safety Evaluator				
Aldara	Safety Evaluator				
Altacor	Safety Evaluator				
Alkeran	Safety Evaluator				
Veltin	Safety Evaluator				
Lutera	Safety Evaluator				

Our analysis of the 53 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics for the names identified in Table 1 above. We determined all 53 names will not pose a risk for confusion as described in Appendix D through E.

DMEPA communicated these findings to the Division of Gastroenterology and Inborn Error Products via e-mail on November 15, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Gastroenterology and Inborn Error Products on October 25, 2011, they stated no additional concerns with the proposed proprietary name, Ultresa.

3 CONCLUSIONS

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

The proposed proprietary name, Ultresa, must be re-reviewed upon submission of the NDA and 90 days before approval of the NDA.

If you have further questions or need clarifications, please contact Nitin Patel, OSE project manager, at 301-796-5412.

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 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.¹

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

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

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

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

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

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

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

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

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

² Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Look-alike		Identical infix Identical suffix Length of the name Overlapping product characteristics	in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and

Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (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.³ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix B1 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

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

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

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

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

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

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

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

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

- a. 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 with possible orthographic or phonetic misinterpretation

Letters	Scripted may appear as	Spoken may be interpreted as
Capital letter 'U'	'L', 'N', 'W', 'M', 'A', 'V', 'O', 'le', 'li'	Any vowel
Lower case 'u'	'n', 'y', 'v', 'w', 'e'	Any vowel
Lower case 'l'	'b', 'e', 's', 'c', 'A', 'P', 'i'	'n'
Lower case 't'	'r', 'f', 'x', 'A'	'd'
Lower case 'r'	's', 'n', 'e', 'v'	'wr'
Lower case 'e'	'a', 'i', 'l', 'p', 'u'	Any vowel
Lower case 's'	'G', 'S', 'g', 'n', 'a'	'c', 'z'
Lower case 'a'	'el', 'ci', 'cl', 'd', 'o', 'u'	Any vowel

Appendix C: FDA Prescription Simulation Samples and Results

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order</u></p> <p><i>Ultresa 20,700 units 7 capsule po</i></p> <hr/> <p><u>Out patient Prescription</u></p> <p><i>Ultresa 13,800 units #270</i> <i>3 capsules TID with meals</i></p> <hr/>	<p>Ultresa 13,800 units 3 capsules po tid with meals #270</p>

Table 1: Prescription Simulation Responses (23 responses on 10/14/11)

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Ultresa	Ultresa	Altresa
Ultresa	Ultresa	Ultresa
Ultresa	Ultresa	Ultresa
Ultresa	Ultresa	
Ultresa 20	Ultresa	
Ultrexa		

Appendix D: Names eliminated from further evaluation for reasons listed below

Proprietary Name		Similarity to Ultresa	Active Ingredient	Reason Eliminated
1	Ultrasex	Look	Multi-ingredient	Dietary supplement containing Yohimbe extract and other ingredients. This product has been discontinued by the manufacturer (found in the Natural Medicine database).
2	UltraAC	Look	Multi-ingredient	Dietary supplement containing Synephrine. Discontinued by the manufacturer (found in the Natural Medicine database).
3	Ultreon	Look	Azithromycin	Product of Germany and South Africa by Pfizer (found in Saegis database).
4	Altrevin	Look	Unknown	Preparations for destroying and combating vermin, fungicides, herbicides, and pesticides. Pending intent to use (found in Saegis database).
5	(b) (4)	Look and sound	Unknown	Not found in any of the available databases including Saegis.
6	Ultreya	Look and sound	Unknown	Categorized as cosmetics, namely perfume, body oils, skin lotion, and disinfectant for air. Abandoned in the US and Canada. Registered in Mexico and Spain (found in Saegis database).
7	Ultrex	Look	Unknown	Categorized as medical supplies. Gel wound dressing with Acemannan by Carrington Laboratories.
8	(b) (4)***	Look	Lubiprostone	Lacks orthographic or phonetic similarity to Ultresa. (b) (4)

*** This is proprietary and confidential information that should not be released to public

Proprietary Name		Proprietary Name	Similarity to Ultresa	Active Ingredient
9	Elestrin	Sound	Estradiol	Lacks orthographic or phonetic similarity.
10	(b) (4)***	Look	Rufinamide	Lacks orthographic or phonetic similarity to Ultresa. Additionally, it is not clear if the name was reviewed by DMEPA (RCM #2008-1502). The name Banzel was found acceptable, and approved for this product in OSE Review #2008-1320, dated October 16, 2008.
11	Isentress (b) (4)	Look and sound	Raltegravir Potassium	Lacks orthographic or phonetic similarity to Ultresa.
12	Trinessa (b) (4)	Look and sound	Norgestimate and Ethinyl Estradiol	Lacks orthographic or phonetic similarity to Ultresa.
13	Verdeso (b) (4)	Look and sound	Desonide	Lacks orthographic or phonetic similarity to Ultresa.
14	(b) (4)			
15	Altracin	Look and sound	Bacitracin	Identified on orphan drug website, but further information not found using other drug references.
16	Ultair***	Look	Pranlukast	Product not available in the US. Trade name is registered in several countries such as Mexico, Argentina, Columbia, Rurguay, Venezuela, Austria, Croatia, Denmark,...
17	Altraco***	Look	Not Applicable	Not a drug name. Identified as 'International Import/Export Business' in Saegis.

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Proprietary Name		Proprietary Name	Similarity to Ultrasa	Active Ingredient
18	Ultima (b) (4)	Look and Sound	Unknown	Identified as a similar name to Ultrasa in the external study (b) (4) but unable to find further information in drug references. The only information found was 'Ultima Products' in Google (e.g. Ultima Replenisher Electrolyte, Ultima Health Products).
19	Ultrason	Look	Unknown	Identified in Redbook (OTC); a topical cream, unable to find further information in drug references.
20	Afresa***	Look	Insulin inhalation powder	Proposed proprietary name was found unacceptable for this product (NDA 022472) by DMEPA in OSE Review #2007-2449, dated June 30, 2009 due to vulnerability to confusion with the name Apidra. The name Afrezza was found acceptable in OSE Review #2009-1471, dated December 8, 2009. However this Application received a complete response on January 18, 2011.
21	(b) (4)			
22	Ultrane	Look	Not applicable	Name identified in Facts and Comparisons database, however, no information was found about this name in Facts & Comparisons or any other databases. Name may have been mis-spelled (correct spelling is Ultrane which is evaluated in this review).
23	Ulticer	Look	Ranitidine	International brand name for Ranitidine (Hong Kong).

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Proprietary Name		Proprietary Name	Similarity to Ultrasa	Active Ingredient
24	Ultrasul	Look and sound	Sulfamethizole	Name identified in Micromedex (Poisindex-identified as Sulfonamides by Alcon Laboratories) database. No other information could be found in any other databases. Search of the Saegis database did not identify this name as a registered tradename in the US or any other countries.
25	Actiza ***	Look	Clindamycin Phosphate 1% foam	Name was found unacceptable for this product (NDA 21709) in OSE Review #03-0288, dated November 26, 2003 due to vulnerability to name confusion with Acticin, Actiq, Ativan, Ariza***, and Ultiva. The name Evoclin was found acceptable by DMEPA for this product (NDA 50801 (NDA 21709 was administratively converted to NDA 50801 because it is an antibiotic submitted under 505B after 11/21/97 to which section 125 exemptions apply)) in OSE Review #04-230, dated September 23, 2004, and approved on October 22, 2004.
26	Ultrase	Look and sound	Pancrelipase	Refer to Section 1.1 <i>Regulatory History</i>
27	Ultrase MT	Look and sound	Pancrelipase	Refer to Section 1.1 <i>Regulatory History</i>

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Appendix E: Potentially confusing names with orthographic, phonetic or differentiating product characteristics that decrease the risk of medication errors

PROPOSED NAME: Ultresa (Pancrelipase) Capsules	STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion	CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
1 Ultracet (Tramadol and Acetaminophen) Tablet 37.5 mg/325 mg Usual Dose: One tablet every 4 to 6 hours as needed.	Orthographic/Phonetic: Both names share the letter string ‘Ultr-’. Additionally, the letter string ‘-esa’ in Ultresa may appear similar to the letter string ‘-ace-’ in Ultracet when scripted. Phonetically, both names consist of 3 syllables. Additionally, the first syllable ‘Ul-’ is the same in both names, and the second syllable ‘-tre-’ in Ultresa may sound similar to the second syllable ‘-tra-’ in Ultracet when spoken. Route of Administration: Oral Dosage Form: Oral solid Possible Overlap in the Frequency Administration: Both products may be taken 3 times daily. Possible Numerical Overlap in the Usual Dose: One	Orthographic/Phonetic: The upstroke ‘t’ at the end of the name Ultracet gives this name a different shape than Ultresa and can help differentiate the two names when scripted. Phonetically, the last syllable ‘-sa’ in Ultresa vs. ‘-cet’ in Ultracet can help distinguish the two names when spoken. Strength: 3 strengths which have to be identified by the prescribers vs. single strength.

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>2 Ultiva (Remifentanyl) Powder for injection 1 mg, 2 mg, 5 mg Usual Dose: Induction of anesthesia is achieved by administration rate of 0.5 mg/kg/min to 1 mcg/kg/min with a hypnotic or volatile agent for the induction of anesthesia.</p>	<p>Orthographic/Phonetic: Both names share the letter string 'Ult-'. Additionally, the letter string '-esa' in Ultresa may appear similar to the letter string '-iva' in Ultiva when scripted. Phonetically, both names consist of 3 syllables and share the same first syllable 'Ul-'. Additionally, both names end with the sound 'ah'. Also, the third syllable of both names ('sa' vs. 'va') may sound similar when spoken.</p>	<p>Phonetic: The second syllable sounds different and can help differentiate the two names when spoken ('-tre-' in Ultresa vs. '-ti-' in Ultiva). Strength: 13,800, 20,700, and 23,000 Lipase units vs. 1 mg, 2 mg, and 5 mg. Frequency of Administration: With meals vs. once Usual Dose: 500 to 1000 Lipase units/kg/meal with titration to less than 2500 lipase units/kg/meal vs. 0.5 mg/kg/min to 1 mcg/kg/min</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules	STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)	
FAILURE MODE: Name Confusion	CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)	
3	Ultane (Sevoflurane) Inhalation liquid, 250 mL Usual Dose: The usual maintenance dose is 0.5-3% with or without nitrous oxide to maintain surgical anesthesia.	Orthographic: Both names share the letter string ‘Ult-‘. Additionally, the letter string ‘-esa’ in Ultresa may appear similar to the letter string ‘-ane’ when scripted. Overlap in the Route of Administration: Oral	Frequency of Administration: With meals vs. once during surgery Strength: 13,800, 20,700, and 23,000 Lipase units vs. 250 mL. Usual Dose: 500 to 1000 Lipase units/kg/meal with titration to less than 2500 lipase units/kg/meal vs. 0.5 to 3%.
4	Alesse (Ethinyl Estradiol and Levonorgestrel) Tablet, 0.02 mg/0.1 mg Usual Dose: One tablet orally daily.	Orthographic: The letter strings ‘Ul-‘ and ‘- sa’ in Ultresa may appear similar to the letter strings ‘Al- ‘ and ‘-se’ in Alesse when scripted. Additionally, both names share the letter string ‘- es-‘. Route of Administration: Oral Dosage Form: Solid oral dosage form Possible Numerical Overlap in the Usual Dose: One	Orthographic: The upstroke ‘t’ in Ultresa can help differentiate Ultresa from Alesse because it provides a different shape for Ultresa. Frequency of Administration: With meals vs. once daily. Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (0.02 mg/0.1 mg)

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>	
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>5</p>	<p>Altace (Ramipril) Tablets 1.25 mg, 2.5 mg, 5 mg, 10 mg</p> <p>Usual Dose: 2.5 mg to 20 mg per day in a single dose or in 2 equally divided doses.</p>	<p>Orthographic/Phonetic: The letter strings ‘Ult-’ and ‘-esa’ in Ultresa may appear similar to the letter strings ‘Alt-’ and ‘-ace’ in Altace when scripted. Phonetically, the first syllable ‘Ul-’ in Ultresa may sound similar to the first syllable ‘Al-’ in Altace when spoken.</p> <p>Route of Administration: Oral</p> <p>Dosage Form Solid oral dosage form</p> <p>Possible Numerical Overlap in the Usual Dose: One</p>	<p>Phonetic: 3 syllables in Ultresa vs. 2 syllables in Altace.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. 1.25 mg, 2.5 mg, 5 mg, and 10 mg.</p> <p>Frequency of Administration: With meals vs. once or twice daily.</p>

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>6 Atreza (Atropine) Tablet 0.4 mg Usual Dose: 0.3 mg to 1.2 mg orally every 4 to 6 hours.</p>	<p>Orthographic/Phonetic: The first letter 'U' and the letter string '-tres-a' in Ultresa may appear similar to the letter 'A' and the letter string '-treza' in Atreza, respectively, when scripted. Phonetically, both names consist of 3 syllables. Additionally, the letter string '-tres-a' in Ultresa may sound similar to the letter string '-treza' in Atreza when spoken.</p> <p>Route of Administration: Oral</p> <p>Dosage Form: Solid oral dosage form</p> <p>Possible Overlap in the Frequency of Administration: Both products may be taken 3 times daily.</p> <p>Possible Numerical Overlap in the Usual Dose: One</p>	<p>Orthographic/Phonetic: The additional upstroke 'l' in Ultresa and the letter 'z' in Atreza (if scripted as a downstroke) can provide different shapes for this name pair and help differentiate the two names when scripted. Phonetically, the first syllable may help differentiate the two names when spoken ('Ul-' vs. 'At-').</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (.4 mg)</p>

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>7 Vitrase (Hyaluronidase) Powder for injection, solution for injection 6,200 units lyophilized powder for injection, 200 units/mL solution for injection Usual Dose: Given one time under specific conditions. Usually 50 to 300 units (most typically 150 units) intravenously.</p>	<p>Orthographic: The letter strings ‘Ul-’ and ‘-tresa’ in Ultresa may appear similar to the letter strings ‘Vi-’ and ‘-trase’ in Vitrase respectively, when scripted.</p>	<p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. 6,200 units or 200 units/mL Frequency of Administration: With meals vs. once Usual Dose: 500 to 1000 Lipase units/kg/meal with titration to less than 2500 lipase units/kg/meal vs. 50 to 300 units.</p>

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>	
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>8</p>	<p>Valtrex (Valacyclovir) Tablets, 500 mg, 1 gram</p> <p>Usual Dose: 500 mg to 1 gram two to three times daily for 5 to 14 days (the length of treatment varies based on the type of injection).</p>	<p>Orthographic: Both names consist of seven letters and share the letter string '-ltre-'. Additionally, the letter 'U' and the letter 'a' in Ultresa may appear similar to the letter 'V' and the letter 'x' in Valtrex, respectively, when scripted.</p> <p>Route of Administration: Oral</p> <p>Dosage Form: Solid oral dosage form</p> <p>Overlap in the Frequency of Administration: 3 times daily</p> <p>Possible Numerical Overlap in the Usual Dose: One or 500</p>	<p>Orthographic: The position of the upstrokes 'l' and 't' is different in the two names due to the presence of the letter 'a' in Valtrex, and can help differentiate the two names when scripted.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. 500 mg and 1 gram.</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
9	Voltaren (Diclofenac) Tablets 25 mg, 50 mg, 75 mg Usual Dose: 100 mg to 125 mg per day in divided doses.	Orthographic: Both names share the upstrokes 'l' and 't'. Additionally, the letter 'U' and the letter string '-res-' in Ultresa may appear similar to the letter 'V' and the letter string '-ren' in Voltaren, respectively, when scripted. Route of Administration: Oral Dosage Form: Solid oral dosage form Possible Overlap in the Frequency of Administration: 3 times. Possible Numerical Overlap in the Usual Dose: One	Orthographic: The position of the upstrokes 'l' and 't' is different in the two names due to the presence of the letter 'o' in Voltaren, and can help differentiate the two names when scripted. Strength: 13,800, 20,700, and 23,000 Lipase units vs. 25 mg, 50 mg, and 75 mg.

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
10	Ultravate (Halobetasol) Cream or ointment 0.05% Usual Dose: Apply to the affected area(s) one to two times daily.	Orthographic: Both names share the letter string 'Ultr-'. Additionally, the letter string '-esa' in Ultresa may appear similar to the letter string '-ava-' in Ultravate when scripted. Possible Numerical Overlap in the Usual Dose One capsule vs. one application	Orthographic: The upstroke 't' in the 8 th position of the name Ultravate provides a different shape for this name than Ultresa and can help differentiate the two names when scripted. Additionally, the name Ultravate appears longer than the name Ultresa when scripted due to the extra letters 't' and 'e' in Ultravate. Route of Administration: Oral vs. topical Dosage Form: Capsules vs. cream or ointment Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (0.5%). Frequency of Administration With meals vs. one to two times daily.

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
11	<p>Ultravist (Iopromide) Solution for injection 623.4 mg/mL (Iodine 300 mg) or 768.86 mg/mL (Iodine 370 mg)</p> <p>Usual Dose: The volume and rate of injection of the contrast agent will vary depending on the injection site and the area being examined. Inject contrast at rates approximately equal to the flow rate in the vessel being injected. Cerebral Arteriography (300 mg I/mL), Coronary Arteriography and Left Ventriculography (370 mg I/mL), Peripheral Arteriography (300 mg I/mL), Aortography and Visceral Angiography (370 mg I/mL): Use a volume and rate of contrast injection proportional to the blood flow and related to the vascular and pathological characteristics of the specific vessels being studied. Do not exceed 225 mL as total dose for the procedure</p>	<p>Orthographic: Both names share the letter string 'Ultr-'. Additionally, the letter string '-esa' in Ultresa may appear similar to the letter string '-avi-' in Ultravist when scripted.</p>	<p>Orthographic: The upstroke 't' at the end of the name Ultravist gives this name a different shape and can help differentiate Ultravist from Ultresa. Additionally, the name Ultravist may appear longer when scripted due to the extra letters 's' and 't' in Ultravist.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. 623.4 mg/mL (or 300 mg) and 768.86 mg/mL (or 370 mg)</p> <p>Frequency of Administration: With meals vs. once</p> <p>Usual Dose: 500 to 1000 Lipase units/kg/meal with titration to less than 2500 lipase units/kg/meal vs. 300 mg or 370 mg.</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
12	<p>Ultracef (Cefadroxil) Capsules and oral suspension 500 mg, 1 gram, 125 mg/5 mL, 250 mg/5 mL, 500 mg/5 mL</p> <p>Usual Dose: 125 mg to 500 mg once or twice daily.</p>	<p>Orthographic/Phonetic Both names share the letter string 'Ultr-'. Additionally, the letter string '-esa' in Phonetically, both names consist of 3 syllables and share the same first syllable Ultresa may appear similar to the letter string '-ace-' in Ultracef when scripted. ('UI-'). Additionally, the second syllable in Ultresa ('-tre-') may sound similar to the second syllable in Ultracef ('-tra-') when spoken.</p> <p>Route of Administration: Oral</p> <p>Overlap in the Dosage Form: Solid oral dosage form</p> <p>Possible Numerical Overlap in the Usual Dose: One or 500</p>	<p>Orthographic/Phonetic: The upstroke 'f' in Ultracef provides a different shape for this name and can help differentiate Ultracef from Ultresa. Additionally, the name Ultracef may appear longer than Ultresa when scripted due to the extra letter 'f' at the end of the name Ultracef.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. 500 mg, 1 gram, 125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL</p> <p>Frequency of Administration: With meals vs. once or twice daily.</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
13	<p>Ultratag (Kit for the preparation of technetium tc 99m-labeled red blood cells) Kit</p> <p>Usual Dose: The suggested dose range of technetium Tc 99m-labeled red blood cells in the average patient (70 kg) is 370 MBq (10 mCi) to 740 MBq (20 mCi) intravenously.</p>	<p>Orthographic: Both names share the letter string 'Ultr-'. Additionally, the letter 'e' in Ultresa may appear similar to the letter 'a' in Ultratag when scripted. Also, both names share the letter 'a' in the seventh position.</p> <p>Possible Numerical Overlap in the Usual Dose: 500 to 100 Lipase units vs. 370 MBq to 740 MBq.</p>	<p>Orthographic: The upstroke 't' in the sixth position of Ultratag and the downstroke 'g' in Ultratag provide a different shape for this name and can help differentiate Ultratag and Ultresa when scripted. Additionally, the name Ultratag appears longer than the name Ultresa when scripted due to the extra letter 'g' in Ultratag.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength</p> <p>Frequency of Administration: With meals vs. once</p>

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>	
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>14</p>	<p>Valturna (Aliskiren Hemifumarate and Valsartan) Tablet 150 mg/160 mg and 300 mg/320 mg</p> <p>Usual Dose: One tablet orally daily, with a routine pattern with regard to meals.</p>	<p>Orthographic: Both names share the upstroke letters 'l' and 't' and end with the letter 'a'. Additionally, the letters 'U', 'r', and 's' in Ultresa may appear similar to the letters 'V', 'u', and 'n' in Valturna, respectively, when scripted.</p> <p>Route of Administration: Oral</p> <p>Dosage Form: Solid oral dosage form</p> <p>Possible Numerical Overlap in the Usual Dose: One</p>	<p>Orthographic: The position of the upstrokes 'l' and 't' is different in the two names due to the presence of the letter 'a' in Valturna, and can help differentiate the two names when scripted.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. 150 mg/160 mg and 300 mg/320 mg</p> <p>Frequency of Administration: With meals vs. once daily.</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
15	Uloric (Febuxostat) Tablet 40 mg, 80 mg Usual Dose: One tablet orally once a day.	Orthographic: Both names share the letter string 'Ul-' and the letter 'r' in the fourth position. Additionally, the letters 'e' and 'a' in Ultresa may appear similar to the letters 'i' and 'c' in Uloric, respectively, when scripted. Route of Administration: Oral Dosage Form: Solid oral dosage form Possible Numerical Overlap in the Usual Dose: One	Orthographic: The upstroke 't' in Ultresa gives this name a different shape than Uloric and can help differentiate Ultresa and Uloric when scripted. Strength: 13,800, 20,700, and 23,000 Lipase units vs. 40 mg and 80 mg. Frequency of Administration: With meals vs. once a day.

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>	
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>16</p>	<p>Ultracal (Multi-ingredient nutritional supplement containing calcium and vitamin D.)</p> <p>Usual Dose: The suggested dose is two tablets orally twice daily.</p>	<p>Orthographic: Both names share the letter string 'Ultr-'. Additionally, the letter string '-esa' in Ultresa may appear similar to the letter string '-aca-' in Ultracal when scripted.</p> <p>Route of Administration: Oral</p> <p>Dosage Form: Solid oral dosage form</p> <p>Possible Overlap in the Frequency of Administration: With meals or 3 times daily (since Ultracal is a nutritional supplement, patients may be told to take with meals.)</p> <p>Possible Numerical Overlap in the Usual Dose: One (since Ultracal is a nutritional supplement, it may be taken as one tablet.)</p>	<p>Orthographic: The upstroke 'l' in the 8th position of Ultracal gives this name a different shape and can help differentiate Ultresa and Ultracal when scripted. Additionally, the name Ultracal appears longer than the name Ultresa when scripted due to the extra letter 'l' in Ultracal.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength.</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
17	Abreva (Docosanol) Cream, 10% Usual Dose: Apply to affected area(s) five times a day until healed for up to 10 days.	Orthographic: The letter string '-tres-a' in Ultresa may appear similar to the letter string ('-brev-a' in Abreva when scripted. Additionally, the letter 'U' in Ultresa may appear similar to the letter 'A' in Abreva when scripted. Possible Numerical Overlap in the Frequency of Administration: 3 times daily (Abreva may be applied 3 times daily) Possible Numerical Overlap in the Usual Dose: One (one application vs. one capsule)	Orthographic: The upstroke 't' in Ultresa gives this name a different shape than Abreva and can help differentiate the two names when scripted. Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (10%).

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>18 (b) (4) ** (Tretinoin) Gel 0.05%</p> <p>(NDA 022070, RCM #2007-1164, the name was not reviewed by DMEPA, however, the name Atralin was found acceptable for this product by DMEPA in OSE Review #2207-1163, dated June 5, 2007.)</p> <p>Usual Dose: Apply thin layer to affected areas once daily before bedtime.</p>	<p>Orthographic: The letter string 'Ultres-' in Ultresa may appear similar to the name (b) (4) when scripted.</p> <p>Possible Numerical Overlap in the Usual Dose: One (one capsule vs. one application)</p>	<p>Orthographic: The name Ultresa may appear longer than the name (b) (4) when scripted due to the extra letter 'a' in Ultresa.</p> <p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (0.05%)</p> <p>Frequency of Administration: With meals vs. once daily before bedtime.</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
19	Altavera (Levonorgestrel and Ethinyl Estradiol) Tablet 0.15 mg/0.03 mg Usual Dose: One tablet orally daily.	Orthographic: The letter strings 'Ult-' and '-resa' in Ultresa may appear similar to the letter strings 'Alt-' and '-vera' in Altavera, respectively, when scripted. Route of Administration: Oral Dosage Form: Solid oral dosage form Possible Numerical Overlap in the Usual Dose: One	Orthographic: The name Altavera may appear longer than the name Ultresa when scripted because of the extra letter 'a' in Altavera. Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (0.15 mg/0.03 mg) Frequency of Administration: With meals vs. once daily.

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>	
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>20</p>	<p>Ultram (Tramadol) Tablet, 50 mg</p> <p>Usual Dose: One tablet every 4 to 6 hours as needed.</p>	<p>Orthographic: Both names share the letter string 'Ultr-'. Additionally, the letter string '-esa' in Ultresa may appear similar to the letter string '-am' in Ultram when scripted.</p> <p>Route of Administration: Oral</p> <p>Dosage Form: Solid Oral dosage form</p> <p>Possible Overlap in the Frequency of Administration: Both products may be taken 3 times daily.</p> <p>Possible Numerical Overlap in the Usual Dose: One</p>	<p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (50 mg).</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
21	Ultram ER (Tramadol) Extended-release tablets 100 mg, 200 mg, 300 mg Usual Dose: 100 mg to 300 mg once daily.	Orthographic: Both names share the letter string 'Ultr-'. Additionally, the letter string '-esa' in Ultresa may appear similar to the letter string '-am' in Ultram when scripted. Route of Administration: Oral Dosage Form: Solid Oral dosage form Possible Numerical Overlap in the Usual Dose: One	Orthographic: If included, the modifier ER may help differentiate the two names. Strength: 13,800, 20,700, and 23,000 Lipase units vs. 100 mg, 200 mg, and 300 mg. Frequency of Administration: With meals vs. once daily.

<p>PROPOSED NAME: Ultresa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>	
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>22</p>	<p>Aldara (Imiquimod) Cream 5%</p> <p>Usual Dose: Actinic Keratosis: Apply twice per week for a full 16 weeks. Superficial basal cell carcinoma: Apply five times per week for a full six weeks. External genital warts: Apply 3 times per week until total clearance or a maximum of 16 weeks.</p>	<p>Orthographic: The letter string 'Ult-' and '-esa' in Ultresa may appear similar to the letter string 'Ald-' and '-ara' in Aldara, respectively, when scripted.</p> <p>Possible Numerical Overlap in the Frequency of Administration: 3 times</p> <p>Possible Numerical Overlap in the Usual Dose: One (one capsule vs. one application)</p>	<p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (5%).</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
23	Altocor (Lovastatin) Extended-release Tablets 20 mg, 40 mg, 60 mg Usual Dose: 20 mg to 60 mg orally once a day in the evening at bedtime.	Orthographic: Both names consist of seven letters. Additionally, the letter string 'Ult-' and the letter 'e' in Ultresa may appear similar to the letter string 'Alt-' and the letter 'c' in Altocor, respectively, when scripted. Route of Administration: Oral Dosage Form: Solid oral dosage form Possible Numerical Overlap in the Usual Dose: One	Strength: 13,800, 20,700, and 23,000 Lipase units vs. 20 mg, 40 mg, and 60 mg Frequency of Administration: With meals vs. once a day in the evening.

<p>PROPOSED NAME: Ultrasa (Pancrelipase) Capsules</p>	<p>STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units</p>	<p>USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)</p>
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>24 Alkeran (Melphalan Hydrochloride) Kit 50 mg Usual Dose: The usual IV dose is 16 mg/m². Dosage reduction of up to 50% should be considered in patients with renal insufficiency (BUN ≥30 mg/dL). The drug is administered as a single infusion over 15 to 20 minutes. Melphalan is administered at 2-week intervals for 4 doses, then, after adequate recovery from toxicity, at 4-week intervals.</p>	<p>Orthographic: Both names consist of seven letters. Additionally, the letter strings 'Ult-' and '-res-' in Ultrasa may appear similar to the letter strings 'Alk-' and '-ran' in Alkeran, respectively, when scripted.</p>	<p>Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (50 mg). Frequency of Administration: With meals vs. every 2 or 4 weeks. Usual Dose: 500 to 1000 Lipase units/kg/meal with titration to less than 2500 lipase units/kg/meal vs. 16 mg/m².</p>

PROPOSED NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
25	Veltin (Clindamycin Phosphate and Tretinoin) Gel 1.2%/0.025% Usual Dose: Apply a pea size amount once daily in the evening lightly covering the entire affected area.	Orthographic: Both names share the upstroke letters 'l' and 't'. Additionally, the letter 'U' and the letter string '-es-' in Ultresa may appear similar to the letter 'V' and the letter string '-in' in Veltin when scripted. Possible Numerical Overlap in the Usual Dose: One (one capsule vs. one application)	Orthographic: The position of the upstrokes 'l' and 't' is different in the two names due to the presence of the letter 'e' in Veltin, and can help differentiate the two names when scripted. Strength: 13,800, 20,700, and 23,000 Lipase units vs. single strength (1.2%/0.025%) Frequency of Administration: With meals vs. once daily in the evening.

NAME: Ultresa (Pancrelipase) Capsules		STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized) PROPOSED
26	Lutera Ethinyl Estradiol and Levonorgestrel 0.02 mg/0.1 mg Usual Dose: One tablet orally daily.	Orthographic: The letter strings 'Ult-' and '-esa' in Ultresa may appear similar to the letter strings 'Lut-' and '-era' in Lutera respectively, when scripted. Route of Administration: Oral Dosage Form: Oral solid dosage form Possible Numerical Overlap in the Usual Dose: One	Strength: 13,800, 20,700, and 23,000 Lipase units vs. Single strength (0.02 mg/0.1 mg) Frequency of Administration: With meals vs. once daily.

NAME: Ultresa (Pancrelipase) Capsules	STRENGTH: Lipase/Amylase/Protease 13,800/27,600/27,600 USP units 20,700/41,400/41,400 USP units 23,000/46,000,46,000 USP units	USUAL DOSE: A starting dose of 500 Lipase USP units/kg/meal to 1000 Lipase USP units/kg/meal with titration to less than 2500 Lipase USP units/kg/meal or less than 4000 Lipase USP units/g fat/day is recommended. (Dosed based on Lipase USP units)
FAILURE MODE: Name Confusion	CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized) PROPOSED
27	<div style="text-align: right;">(b) (4)</div>	

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/s/

MANIZHEH SIAHPOUSHAN
12/05/2011

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

Date: October 2, 2009

To: Donna Griebel, MD
Director, Division of Gastroenterology Products

Through: Todd Bridges, RPh, Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Denise V. Baugh, PharmD, BCPS, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Ultresa (Pancrelipase) Capsules
13,800 USP units of lipase, 27,600 USP units of amylase and
27,600 USP units of protease;
20,700 USP units of lipase; 41,400 USP units of amylase and
41,400 USP units of protease;
23,000 USP units of lipase, 46,000 USP units of amylase and
46,000 USP units of protease

Application Type/Number: NDA# 022222

Applicant: Axcan Pharma US, Inc

OSE RCM #: 2009-1286

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CONTENTS

EXECUTIVE SUMMARY	3
1 BACKGROUND	3
1.1 Introduction.....	3
1.2 Regulatory History	3
1.3 Product Information	3
2 METHODS AND MATERIALS	4
2.1 Search Criteria.....	4
2.2 FDA Prescription Analysis Studies.....	4
2.3 External Proprietary Name Risk Assessment	5
3 RESULTS.....	6
3.1 Database and Information Sources.....	6
3.2 CDER Expert Panel Discussion.....	6
3.3 FDA Prescription Analysis Studies.....	6
3.4 External Proprietary Name Risk Assessment	6
3.5 Comments from the Division of Gastroenterology Products (DGP)	7
3.6 Safety Evaluator Risk Assessment.....	7
4 DISCUSSION	7
5 CONCLUSIONS AND RECOMMENDATIONS	7
5.1 Comments To The Applicant.....	7
6 REFERENCES	8
APPENDICES	10

EXECUTIVE SUMMARY

Ultresa is the proposed proprietary name for Pancrelipase Capsules. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name Ultresa conditionally acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

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

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Axcan Pharma US, Inc. received on July 7, 2009, for an assessment of the proposed proprietary name, Ultresa, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, the Applicant submitted an external evaluation of the proposed proprietary name.

1.2 REGULATORY HISTORY

Ultrase MT12, Ultrase MT18 and Ultrase MT20 have been marketed without an approved NDA since October, 1991. In response to the “Guidance for Industry: Exocrine Pancreatic Insufficiency Drug Products – Submitting NDAs” dated April, 2006, the Applicant has submitted an NDA for approval. The Agency regulatory history of this product is as follows:

- May 30, 2008 - DMEPA evaluated the name, Ultrase MT previously (OSE# 2007-1913) and found the name vulnerable to confusion with the trademarked name, Altace and the parent drug Ultrase in addition to containing letter and numeric suffixes that could lead to medication errors. Furthermore, we objected to the name because it contained the United States Adopted Names (USAN) stem, “-ase”.
- March 12, 2009 - The Applicant submitted three new names (Ultrase MT 13,800, Ultrase MT 20,700 and Ultrase MT 23,000) and three alternative names (Ultrase 13,800, Ultrase 20,700 and Ultrase 23,000). DMEPA objected to the use of these names (correspondence dated June 10, 2009) due to the inclusion of a USAN stem in the proprietary name and unacceptable modifiers.

1.3 PRODUCT INFORMATION

Ultresa is an orally administered pancreatic enzyme product prescribed to improve digestion of food, especially fat and is indicated for the treatment of patients with exocrine pancreatic insufficiency caused by cystic fibrosis, chronic pancreatitis, or other related conditions. The dose is individualized and determined by the degree of steatorrhea present and the fat content of the diet. Therapy should start at the lowest possible dose and gradually increase until the desired control of symptoms is obtained. A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended. Doses in excess of 6,000 lipase USP units/kg/meal have been associated with fibrosing colonopathy. Ultresa will be available in the following three formulations in bottles of 100 and 500:

- 1) 13,800 USP units of lipase, 27,600 USP units of amylase and 27,600 USP units of protease;
- 2) 20,700 USP units of lipase; 41,400 USP units of amylase and 41, 400 USP units of protease; and
- 3) 23,000 USP units of lipase, 46,000 USP units of amylase and 46,000 USP units of protease.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

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

To identify drug names that may look similar to Ultresa, the DMEPA staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (7 letters), upstrokes (3, capital letter ‘U’, lower case ‘l’ and ‘t’), down strokes (0), cross-strokes (one, ‘t’), and dotted letters (0). Additionally, several letters in Ultresa may be vulnerable to ambiguity when scripted (see Appendix B). As such, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Ultresa.

When searching to identify potential names that may sound similar to Ultresa, the DMEPA staff search for names with similar number of syllables (3), stresses (ul-TRES-a or UL-tresa), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered. The Applicant did not provide their intended pronunciation of the proprietary name in the proposed name submission and, therefore, it could not be taken into consideration.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

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

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

Figure 1. Ultresa Prescription Study (conducted on July 28, 2009)

HANDWRITTEN MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> <p><i>Ultresa 13800 units 3 capsules tid with meals</i></p>	<p>“Ultresa 13,800 units Take 3 capsules TID with meals Dispense #270”</p>
<p><u>Outpatient Prescription:</u></p> <p><i>Ultresa 13800 units Take 3 capsules tid w/ meals #270 Dr. <i>DA</i></i></p>	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA’s database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator’s Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

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

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of twenty-six names as having some similarity to the proposed proprietary name Ultresa.

Eighteen of the names were thought to look like Ultresa. These include Ultreon, Ultram, Afresa, Abreva, (b) (4) Actiza, (b) (4) Vitresa, (b) (4) Ultane, Ultracal, Altavera, Voltaren, Vitrase, Ultrasono, Ultair, and Altraco. Two of the names were thought to sound like Ultresa. These include Atreza and Elestrin. The remaining six names were thought to look and sound similar to Ultresa: Ultrase, Ultracet, Ultracef, Ultiva, Altace, and Altracin.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of August 28, 2009.

3.2 CDER EXPERT PANEL DISCUSSION

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

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of twenty-eight practitioners responded but none of the responses overlapped with any existing or proposed drug names. Eighteen of the participants interpreted the name correctly as “Ultresa,” with correct interpretation occurring in the inpatient written study (n = 13) and the outpatient written study (n = 5). The remainder of the responses misinterpreted the drug name. In the inpatient study, one practitioner misinterpreted the name and in the verbal study, four responses were misspelled phonetic variations of the proposed name, Ultresa. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

In the proposed name risk assessment submitted by the Applicant, (b) (4) a subsidiary of (b) (4) identified and evaluated a total of twelve drug names (Alesse, Altace, Atreza, Isentress, Trinessa, Ultima, Ultiva, Ultracet, Ultram, Ultram ER, Ultrase, and Verdeso) thought to have some potential for confusion with the name Ultresa. Six of these names (Altace, Ultiva, Ultracet, Ultram, Atreza and Ultrase) were also identified by DMEPA during the database searches. The six remaining names were evaluated as part of the Safety Evaluator Risk Assessment.

3.5 COMMENTS FROM THE DIVISION OF GASTROENTEROLOGY PRODUCTS (DGP)

In response to an e-mail from OSE dated July 22, 2009, the Division of Gastroenterology Products did not forward any comments and/or concerns about the proposed name at the initial phase of the name review.

DMEPA notified the Division of Gastroenterology Products via e-mail that we had no objections to the proposed proprietary name, Ultresa, on September 17, 2009. Per e-mail correspondence from the Division of Gastroenterology Products on September 25, 2009, they indicated they concur with our assessment of the proposed proprietary name, Ultresa.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator did not identify any additional names which were thought to look or sound similar to Ultresa and represent a potential source of drug name confusion. Additionally, attempts to identify the drug name Vitresa were unsuccessful. We determined this name to be misspelled by one of the safety evaluators. The correct name is Vitrase which was also identified during the database search, and this name was evaluated further.

4 DISCUSSION

Neither DDMAC nor the review Division had concerns with the proposed name.

DMEPA identified and evaluated thirty-one names for their potential similarity to the proposed name, Ultresa. Six names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix D).

Failure mode and effect analysis (FMEA) was then applied to determine if the potential name could potentially be confused with the remaining twenty-five names and lead to medication errors. This analysis determined that the name similarity between Ultresa and the remaining twenty-five products was unlikely to result in medication errors for the reasons presented in Appendices E through K.

Additionally, DMEPA did not identify any other factors outside of identifying potentially similar or promotional names that would render the name unacceptable at this time. This finding is consistent with the independent name study.

5 CONCLUSIONS AND RECOMMENDATIONS

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

However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. The proposed name must be re-reviewed 90 days before approval of the NDA. For questions or clarifications, please contact OSE Project Manager Phuong (Nina) Ton, at 301-796- 1648.

5.1 COMMENTS TO THE APPLICANT

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

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

6 REFERENCES

1. *OSE Review # 2007-1913 Proprietary Name, Label and Labeling Review for Ultrase MT 12 (Pancrelipase) capsules containing 13,800 USP units of lipase, 27,600 USP units of amylase and 27,600 USP units of protease; Ultrase MT18 (Pancrelipase) Capsules containing 20,700 USP units of lipase, 41,400 USP units of amylase and 41400 USP units of protease; and Ultrase MT20 (Pancrelipase) Capsules containing 23,000 USP units of lipase, 46,000 USP units of amylase and 46,000 USP units of protease, Baugh, D.; May 30, 2008.*

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

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

3. *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.

4. *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.

5. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in review divisions.

6. *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.

7. *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.

8. *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.

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

USPTO provides information regarding patent and trademarks.

10. 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.

11. 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.

12. 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.

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

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

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

USAN Stems List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

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

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

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

17. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.³

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

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

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

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

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

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

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

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

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

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

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

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

1. Database and Information Sources

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

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND Review Division or Office of Generic Drugs

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

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

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

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

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

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

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in proposed name, Ultresa	Scripted may appear as	Spoken may be interpreted as
Capital ‘U’	W, V, O, N	Any vowel
lower case ‘l’	e, b, t	
lower case ‘t’	x, r, f, k, l	ch
lower case ‘r’	n, v, s	
lower case ‘e’	l, a, u, i, o	Any vowel
lower case ‘s’	g, n	x, z, f, c
lower case ‘a’	c, d, o, ‘-ci-’, ‘-ce-’ or ‘-cl-’	Any vowel
Combination letters ‘tr’	Combination letters ‘br’	Combination letters ‘-chr-’
Combination letters ‘re’	u	

Appendix C: FDA Prescription Study Responses.

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Ultresa	Ultrese	Ultressa
Ultresa	Ultrese	Altresa
Ultresa	Ultresa	Ultressa
Ultresa	Ultresse	Oltresa
Ultresa (too similar to Ultrase)	Ultrea	
Ultresa	Ultresa	
Ultresa	Ultress	
Ultressa		
Ultresa		
Ultresa		
Ultresa		

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

Name	Similarity to Ultresa
(b) (4) ***	Look
Elestrin	Sound
(b) (4) ***	Look
Isentress (b) (4)	Look or Sound
Trinessa (b) (4)	Look or Sound
Verdeso (b) (4)	Look or Sound

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

Appendix E: Names which are not drugs.

Proprietary Name	Similarity to Ultresa	Description
Ultracal (Liquid)	Look	Nutritional supplement

Appendix F. Drug names not approved by the Agency

Proprietary Name	Similarity to Ultresa	Comments
(b) (4)		

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

Appendix G: Proprietary or Established Names used only in Foreign Countries

Proprietary Name	Similarity to Ultresa	Country
Ultreon (azithromycin)	Look	Germany

Appendix H: Drug products not found in commonly referenced databases (See Section 6, References 1 through 16)

Name	Similarity to Ultresa	Comments
Altracin (bacitracin)	Look and Sound	Identified on orphan drug website, but further information not found using other drug references
Ultair ***	Look	Identified in DSS database, but further information not found using other drug references
Altraco ***	Look	Identified in DSS database, but further information not found using other drug references
Ultima	Look or Sound (b) (4)	Identified as a similar name to Ultresa in the external study (b) (4) but unable to find further information in drug references
Ultrasone	Look	Identified in Redbook (OTC); a topical cream, unable to find further information in drug references

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

Appendix I: Products with no numerical overlap in strength and dose

Product name with potential for confusion	Similarity to Ultresa	Strengths (USP units of lipase, amylase and protease)	Usual Dose
Ultresa		13,800/27,600/27,600; 20,700/41,400/41,400; and 23,000/46,000/46,000 Dosing is based upon lipase content	A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended.
Voltaren (diclofenac) 25 mg, 50 mg delayed release tablet	Look	25 mg, 50 mg, 75 mg	100 mg to 125 mg/day in divided doses
Ultiva (Remifentanyl)	Look and	1 mg, 2 mg, 5 mg	Induction of anesthesia is achieved by administration of an infusion rate of

Product name with potential for confusion	Similarity to Ultresa	Strengths (USP units of lipase, amylase and protease)	Usual Dose
Ultresa		13,800/27,600/27,600; 20,700/41,400/41,400; and 23,000/46,000/46,000 Dosing is based upon lipase content	A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended.
powder for injection	Sound		0.5 mg/kg/min to 1 mcg/kg/min with a hypnotic or volatile agent for the induction of anesthesia.
Altace (Ramipril) oral tablets, oral capsules	Look and Sound	1.25 mg, 2.5 mg, 5 mg, 10 mg	2.5 mg to 20 mg/day in a single dose or in 2 equally divided doses
Afresa *** (insulin inhalation powder) 15 unit and 30 unit cartridges	Look	15 unit cartridge delivers 4 units of insulin and the 30 unit cartridge delivers 8 units of insulin	Insulin is individualized and administered by inhalation at each meal

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

Appendix J: Single strength products with different product characteristics which will minimize the potential for medication errors with Ultresa.

Product name with potential for confusion & Similarity to Ultresa (in parenthesis)	Strengths (USP units of lipase, amylase and protease)	Usual Dose (if applicable)	Factors which make confusion with Ultresa unlikely (Ultresa vs. Product)
Ultresa (Pancrelipase) capsule	13,800/27,600/27,600; 20,700/41,400/41,400; and 23,000/46,000/46,000 Dosing is based upon lipase content	A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended.	Units of measurement: units Route of administration: oral Dose: individualized to the patient Dosage form: capsule Frequency of administration: three times a day with meals
Abreva (docosanol) topical cream (Look)	10%	Apply to affected area five times a day until healed for up to 10 days.	Dosage form is cream Route of administration is topical Frequency of administration is 5 times a day Duration of treatment is limited to 10 days Product is over-the-counter and likely to be supplied in the retail pharmacy setting only

Product name with potential for confusion & Similarity to Ultresa (in parenthesis)	Strengths (USP units of lipase, amylase and protease)	Usual Dose (if applicable)	Factors which make confusion with Ultresa unlikely (Ultresa vs. Product)
Ultresa (Pancrelipase) capsule	13,800/27,600/27,600; 20,700/41,400/41,400; and 23,000/46,000/46,000 Dosing is based upon lipase content	A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended.	Units of measurement: units Route of administration: oral Dose: individualized to the patient Dosage form: capsule Frequency of administration: three times a day with meals
Actiza *** (clindamycin Phosphate) Foam (Look)	1%	Apply to affected area once daily and massaged in until the foam disappears	Dosage form is foam Route of administration is topical Frequency of administration is once daily
(b) (4) *** (tretinoin) Gel (Look)	0.05%	Apply thin layer to affected areas once daily before bedtime	Dosage form is gel Route of administration is topical Frequency of administration is once daily
Altavera *** (levonorgestrel and ethinyl estradiol) Tablet (Look)	0.15 mg/ 0.03 mg	One tablet orally daily	A prescription for Ultresa will require specification of a product strength (13,800, 20,700 or 23,000 units of lipase) to dispense or administer the proper dose. Frequency of administration is once daily
Atreza (atropine) oral tablet (Sound and Look)	0.4 mg	0.3 mg to 1.2 mg orally every 4 to 6 hours	A prescription for Ultresa will require specification of a product strength (13,800, 20,700 or 23,000 units of lipase) to dispense or administer the proper dose. Frequency of administration is every 4 to 6 hours for irritable bowel syndrome (Clin Pharm)
Alesse (ethinyl estradiol and levonorgestrel) (Sound and Look (b) (4))	0.02 mg/0.1 mg	One tablet orally daily	A prescription for Ultresa will require specification of a product strength (13,800, 20,700 or 23,000 units of lipase) to dispense or administer the proper dose. Frequency of administration is once daily

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

Appendix K: Potentially confusing names to Ultresa which are unlikely to cause medication errors.

Failure Mode: Name confusion	Causes (could be multiple)	Rationale that minimizes the risk of a medication error
<p>Ultresa</p> <p>Strength (USP units of lipase, amylase and protease)</p>		<p>Usual Dose: A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended. Doses are to be taken with meals.</p>
<p>Vitrase (hyaluronidase) powder for injection, solution for injection</p> <p>6,200 units lyophilized powder for injection;</p> <p>200 units/mL solution for injection</p>	<p>Orthographic similarity stems from the names having similar lengths, the similar appearance of ‘V’ (Vitrase) and ‘U’ (Ultresa) when written, and the fact that both names share the letters ‘-tr-’ and ‘s’ in similar positions.</p> <p>Similarities in product characteristics include the use of the same units of measurements (units).</p>	<p>Medication error is unlikely to occur because Vitrase is given one time under specific conditions (absorption and dispersion of other injected drugs); the dose is not weight based (usually 50 to 300 units, most typically 150 units is given); and the route of administration is intravenous. This differs from Ultresa which is given chronically, the dose is individualized to the patient and the route of administration is oral.</p>
<p>Ultrase (Pancrelipase) capsules</p> <p>4,500/20,000/25,000</p> <p>Dosing is based upon lipase content</p>	<p>Orthographic similarity stems from sharing the same five letters in the same position (ULTRASE vs. ULTRESA). Additionally, although the letters ‘a’ and ‘e’ are in opposite positions, this is unlikely to significantly differentiate these names from each other when written.</p> <p>Ultresa and Ultrase share the same product characteristics and dosing regimen.</p>	<p>We anticipate this product will not be available in the marketplace once Ultresa is approved. Based on the “Guidance for Industry: Exocrine Pancreatic Insufficiency Drug Products-Submitting NDAs” dated April, 2006, market availability of these products must be based upon the submission of an NDA. Since an NDA has not been submitted for Ultrase, it is not anticipated that confusion between Ultrase and Ultresa will occur.</p> <p>Additionally, we note the numerical differences between Ultrase and Ultresa. The dose is based on the lipase component which is 4,500 units while the lipase components of Ultresa are 13,800; 20,700; and 23,000 units. The labeling for Ultresa will also state that there cannot be substitutions on a unit per unit basis. Therefore, the different strengths will minimize confusion between these two products.</p>

Failure Mode: Name confusion	Causes (could be multiple)	Rationale that minimizes the risk of a medication error
Ultresa Strength (USP units of lipase, amylase and protease)		Usual Dose: A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended. Doses are to be taken with meals.
Ultrase MT 12 12,000/39,000/ 39,000 Ultrase MT 18 18,000/58,500/ 58,500 Ultrase MT 20 20,000/65,000/ 60,000 Dosing is based upon lipase content	Orthographic similarity stems from sharing the same five letters in the same position (ULTRASE vs. ULTRESA). Additionally, although the letters ‘a’ and ‘e’ are in opposite positions, this is unlikely to significantly differentiate these names from each other when written. Ultresa and Ultrase share the same product characteristics and dosing regimen	The differing product strengths between Ultrase MT and Ultresa should minimize the likelihood for confusion during the transition period from the currently marketed product to the proposed product. Since dosing is weight based using the lipase content and there are different strengths available, the prescriber will have to indicate the appropriate strength to achieve the intended dose. Additionally, we note some numerical overlap between Ultrase MT 20 (20,000 units of lipase) and Ultresa 20,700 units of lipase). However, the labeling for Ultresa will state that there cannot be substitutions on a unit per unit basis. Therefore, the pharmacist or nurse will have to call the prescriber to ascertain their intentions because the actual amounts differ (20,000 units vs. 20,700 units)..
Ultane (sevoflurane) liquid, inhalation 250 mL	Orthographic similarity stems from having the same initial three letters (‘Ult’) as well as having similar shapes and lengths when written.	Product characteristics differ between this name pair which will likely minimize confusion between Ultane and Ultresa. The dosage form (inhalation liquid vs oral capsule), dose (non-specific vs. weight-based), frequency (during surgical procedure vs. with meals) and practice settings (surgical vs. ambulatory).
Ultracet (tramadol and acetaminophen) tablet 37.5 mg and 325 mg	Orthographic similarity is caused by sharing the same initial four letters (‘Ultr-’). Shared product characteristics include route of administration (oral)	Although this name pair shares the first four letters in their name (ULTR-), Ultracet is distinguishable from Ultresa because of the last letter which is represented by a cross stroke (‘t’) and which also serves to highlight its longer appearance when scripted. Additionally, the units of measurement differ (milligrams vs. USP units) as well as the frequency of administration (every 4 hours to 6 hours vs with meals). Furthermore, since Ultracet is available in a single strength, it is likely that the prescriber will not state the strength on a prescription whereas this information will be required for Ultresa (due to its availability in 3 strengths). Hence, the overall presentation of information (such as strength and frequency of administration) on the prescription order will help to distinguish these drug names from each other.
Ultracef (cefadroxil) oral capsule, oral suspension 500 mg, 1 gram, 125 mg per 5 mL, 250 mg per 5 mL, 500 mg per 5 mL	Orthographic similarity is caused by sharing the same initial four letters (‘Ultr-’).	Although both Ultresa and Ultracef share the first four letters in their name, Ultracef is distinguishable from Ultresa because of the last letter which is represented by an upstroke (‘f’) and which also serves to highlight its longer appearance when scripted. Additionally, the units of measurement (grams or milligrams vs. USP units) and frequency of administration (once or twice daily vs. with meals) differ.

Failure Mode: Name confusion	Causes (could be multiple)	Rationale that minimizes the risk of a medication error
Ultresa Strength (USP units of lipase, amylase and protease)		Usual Dose: A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended. Doses are to be taken with meals.
Ultram (tramadol) oral tablet 50 mg	Orthographic similarity is caused by sharing the same initial four letters ('Ultr-').	Product characteristics differ for these drug products. This includes the strength (50 mg to 100 mg vs. XX units of lipase/kg) and the frequency of administration (every 4 hours to 6 hours as needed vs. three times daily with meals). These differences will minimize the potential for confusion.
Ultram ER (tramadol) Extended-release tablet 100 mg, 200 mg, 300 mg	Orthographic similarity is caused by sharing the same initial four letters ('Ultr-').	The frequencies of administration differ between these drug products (once daily vs. three times daily with meals). Additionally, as both drug products are available in several strengths, the inclusion of this information on a prescription will minimize the potential for confusion.

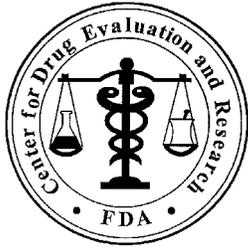
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/s/

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Department of Health and Human Services
Public Health Service
Food and Drug Administration
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Date: May 30, 2008

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Division of Medication Error Prevention

From: Denise V. Baugh, PharmD, BCPS, Safety Evaluator
Division of Medication Error Prevention

Subject: Proprietary Name, Label and Labeling Review

Drug Name(s): Ultrase MT12
(Pancrelipase) Capsules
13,800 USP units of lipase, 27,600 USP units of amylase and
27,600 USP units of protease;

Ultrase MT18
(Pancrelipase) Capsules
20,700 USP units of lipase; 41,400 USP units of amylase and 41,
400 USP units of protease;

Ultrase MT20
(Pancrelipase) Capsules
23,000 USP units of lipase, 46,000 USP units of amylase and
46,000 USP units of protease

Application Type/Number: NDA# 22-222

Applicant: Axcan Pharma US, Inc.

OSE RCM #: 2007-1913

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CONTENTS

EXECUTIVE SUMMARY	1
1 BACKGROUND.....	1
1.1 Introduction.....	1
1.2 Regulatory History	1
1.3 Product Information	1
2 METHODS AND MATERIALS	3
2.1 Proprietary Name Risk Assessment	3
2.2 Label and Labeling Risk Assessment	10
3 RESULTS.....	11
3.1 Proprietary Name Risk Assessment.....	11
3.2 Label and Labeling Risk Assessment	14
4 DISCUSSION	14
4.1 Proprietary Name Risk Assessment.....	14
4.2 Label and Labeling Risk Assessment	Error! Bookmark not defined.
4.3 The Division of Medication Error Prevention’s Response to the External Name Study 17	
4.4 Overlapping Formulations of Ultrase MT – old and new	17
4.5 USAN Stem	18
5 CONCLUSIONS and RECOMMENDATIONS.....	19
5.1 Comments to the Division.....	19
5.2 Comments to the Applicant.....	20
5.3 The Division of Medication Error Prevention’s Response to the External Name Study 22	
5.4 Overlapping Formulations of Ultrase MT – Old and New	23
5.5 USAN Stem	23
5.6 Labels and Labeling.....	24
6 REFERENCES	25
APPENDICES	26

EXECUTIVE SUMMARY

The Proprietary Name Risk Assessment findings indicate that the proposed name, Ultrase MT is vulnerable to name confusion with the trademarked name Altace and the parent drug Ultrase in addition to containing letter and numeric suffixes that could lead to medication errors. Additionally, we note that the proposed proprietary name, Ultrase contains the United States Adopted Names (USAN) stem “-ase”. Although this is the correct stem, the use of this term in the proprietary name is inconsistent with the (USAN) Council’s intent for stems to be reserved for established names only. Thus, the Division of Medication Error Prevention objects to the use of the proposed proprietary name, Ultrase MT, and recommends the Applicant submit two alternative proprietary names for consideration.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Gastroenterology Products for assessment of the proposed proprietary name “Ultrase MT” regarding potential name confusion with other proprietary or established drug names in normal practice settings. Specifically, the proposed names are Ultrase MT12, Ultrase MT18 and Ultrase MT20. Additionally, container labels and carton labeling were provided for review and comment for their potential to contribute to medication error.

1.2 REGULATORY HISTORY

Ultrase MT12, Ultrase MT18 and Ultrase MT20 are currently available in the marketplace without an approved NDA since October, 1991. In response to the “Guidance for Industry: Exocrine Pancreatic Insufficiency Drug Products – Submitting NDAs” dated April, 2006, the sponsor has now revised this NDA for a reformulated Ultrase MT enteric coated mini-tablet for approval.

1.3 PRODUCT INFORMATION

Ultrase MT is an extension of the Ultrase product line. Ultrase MT is an orally administered pancreatic enzyme product prescribed to improve digestion of food, especially fat and is indicated for the treatment of patients with exocrine pancreatic insufficiency caused by cystic fibrosis, chronic pancreatitis, or other related conditions. The dose is individualized and determined by the degree of steatorrhea present and the fat content of the diet. Therapy should start at the lowest possible dose and gradually increase until the desired control of symptoms is obtained. A starting dose of 500 lipase USP units/kg/meal to 1,000 lipase USP units/kg/meal with titration to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day is recommended. Doses in excess of 6,000 lipase USP units/kg/meal have been associated with fibrosing colonopathy.

Currently, the Ultrase MT formulation is: Ultrase MT12 - 12,000 USP units of lipase, 39,000 USP units of amylase and 39,000 USP units of protease; Ultrase MT18 – 18,000 USP units of lipase; 58,500 USP units of amylase and 58,500 USP units of protease; and Ultrase MT20 - 20,000 USP units of lipase, 65,000 USP units of amylase and 65,000 USP units of protease.

The proposed Ultrase MT formulation will be available as: Ultrase MT12 - 13,800 USP units of lipase, 27,600 USP units of amylase and 27,600 USP units of protease; Ultrase MT18 - 20,700 USP units of lipase; 41,400 USP units of amylase and 41,400 USP units of protease; and Ultrase

MT20 - 23,000 USP units of lipase, 46,000 USP units of amylase and 46,000 USP units of protease. See Table 1 on page 3 to compare the content of the new and old formulations.

Additionally, Ultrase MS4 is part of this product line and is available in the marketplace without an approved NDA. Based upon front-line practice experience, Ultrase MS4 is known as ‘Ultrase’ in the marketplace. Because of its shared root name with the proposed proprietary names, we used failure mode and effects analysis (FMEA) to assess the risk for confusion between these names to lead to medication errors in the usual practice settings. See Section 4.1.2 for further details.

Ultrase MS4 dosing should begin with one to two capsules given orally with meals or snacks and the dosage adjusted according to symptoms. The number of capsules or capsule strength given with meals and/or snacks should be estimated by assessing which dose minimizes steatorrhea and maintains good nutritional status. Dosages should be adjusted according to the response of the patient. If swallowing is difficult, the capsules may be opened and the microspheres added to a small quantity of a soft food (eg, applesauce, gelatin, etc.) that does not require chewing, and swallowed immediately. It is recommended that the total dose of pancrelipase be dispersed equally (with fluids) before, during, and after the meal or snack.

Ultrase MT12, Ultrase MT18 and Ultrase MT20 Capsules contain enteric coated mini-tablets. Ultrase MS4 Capsules contain enteric-coated microspheres.

Additionally, we note that per correspondence from the Applicant dated February 14, 2008, the modifier ‘MT’ stands for ‘mini-tablets’ and the ‘MS’ refers to ‘microspheres’. The numerical modifiers (‘4’, ‘12’, ‘18’ and ‘20’) refer to the units of lipase in each capsule. Ultrase MS4 is currently the pediatric formulation prescribed for young patients 0 – 2 years of age.

Table 1. Currently available and Proposed Ultrase MT products.

Current formulations:

	Ultrase MT 12	Ultrase MT18	Ultrase MT 20	Ultrase MS4
Lipase, USP units	12,000	18,000	20,000	4,500
Protease, USP units	39,000	58,500	65,000	20,000
Amylase, USP units	39,000	58,500	65,000	25,000

Proposed formulations:

	Ultrase MT12	Ultrase MT18	Ultrase MT20	(b) (4)
Lipase, USP units	13,800	20,700	23,000	
Protease, USP units	27,600	41,400	46,000	
Amylase, USP units	27,600	41,400	46,000	

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the medication error staff conducting a proprietary name risk assessment (see Section 2.1) and label, labeling, and/or packaging risk assessment (see Section 2.2). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention 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

2.1 PROPRIETARY NAME RISK ASSESSMENT

The Division of Medication Error Prevention is aware that Ultrase MT and Ultrase have coexisted in the marketplace prior to the submission of this NDA for Ultrase MT. As a result of post-marketing experience with similar name pairs, Ultrase MT was assessed as a product line extension of Ultrase. We also considered the risk of confusion between the proposed name, “Ultrase MT” and the root name (“Ultrase”), the letter abbreviations (‘MT’), the numerical modifiers (‘12’, ‘18’, and ‘20’) as well as those pending IND, NDA, and ANDA products currently under review by the Agency. All modifiers were assessed for resemblance to any numbers, dosing instructions, or medical abbreviations. Furthermore, the medication error staff considered the potential for the modifier to be omitted or misinterpreted, confusing or misleading. Our concerns are stated in detail below.

For the root name, ‘Ultrase’, and the letter abbreviations (‘MT’) and numerical modifiers (‘12’, ‘18’, and ‘20’), the medication error staff searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Section 2.1.1) and held a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see Section 2.1.1.2). The Division of Medication Error Prevention also conducts internal CDER prescription analysis studies (see Section 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see Section 2.1.4).

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see Section 2.1.4). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.² FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As

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

² Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

such, the Staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed drug 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, the Division of Medication Error Prevention 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

2.1.1 Search Criteria

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter ‘U’, ‘W’, ‘A’ and ‘V’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.⁴⁵

To identify drug names that *look* similar to Ultrase MT12, Ultrase MT18 or Ultrase MT20 the Staff also considers the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (9 letters, 2 numbers), upstrokes (5, capital letters ‘U’, ‘M’, ‘T’ and lower case ‘l’ and lower case ‘t’), downstrokes (none), cross-strokes (2, ‘t’ and ‘T’), letter modifiers (‘M’, ‘T’) and numerical modifiers (‘12’, ‘18’, and ‘20’). Additionally, several letters in Ultrase MT12, Ultrase MT18 and/or Ultrase MT20 may be vulnerable to ambiguity when scripted, including the capital letter ‘U’ may appear as ‘V’, a ‘W’ or an ‘A’; or the combination capital letter ‘U’ and lower case ‘L’ may appear as a ‘W’; the lower case ‘L’ may appear as a lower case ‘t’, ‘d’, ‘e’, or ‘b’ or vice versa; lower case ‘t’ may appear as an ‘x’; lower case ‘r’ may appear as an ‘n’ or ‘s’; lower case ‘a’ may appear as a lower case ‘c’, ‘e’, ‘u’ or the combination letters ‘-ci’, ‘-ce’, or ‘-el’; and lower case ‘s’ may appear as a lower case ‘n’ or ‘r’. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Ultrase MT12.

When searching to identify potential names that may *sound* similar to Ultrase MT12, Ultrase MT18 and/or Ultrase MT20 the Medication Error Staff focused on the root name, “Ultrase” and searched for names with similar numbers of syllables (2), stresses (UL-trase), ul-TRASE) and placement of vowel and consonant sounds. We also considered how the modifiers, ‘MT’ and ‘12’, ‘18’ and/or ‘20’ may change the sound and thus the interpretation of the name. For example, the first letters of Ultrase (‘UL’) may sound like the word ‘all’, the letter modifiers

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

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

'MT' can sound like the word 'empty', the number modifier '18' (in Ultrase MT18) may sound like the number '80', and the suffix '-ase' may sound like '-ace'. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary names ("Ultrase MT"), the established name (Pancrelipase), proposed indication (treatment of patients with exocrine pancreatic insufficiency), strength (Ultrase MT12 - 13,800 USP units of lipase, 27,600 USP units of amylase and 27,600 USP units of protease; Ultrase MT18 - 20,700 USP units of lipase; 41,400 USP units of amylase and 41,400 USP units of protease; and Ultrase MT20 - 23,000 USP units of lipase, 46,000 USP units of amylase and 46,000 USP units of protease), dose (500 to 1,000 lipase USP units/kg/meal with titration, based on clinical response, to less than 2,500 lipase USP units/kg/meal or less than 4,000 lipase USP units/g fat/day), frequency of administration (with meal), route (oral) and dosage form of the product (gelatin capsules containing enteric coated minitablets). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff generally take into consideration.

Lastly, the Medication Error Staff also considers the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name, "Ultrase MT", was provided to the medication error staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to "Ultrase MT" using the criteria outlined in Section 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review the United States Adopted Names (USAN) stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention to gather CDER professional opinions on the safety of the product and the proprietary name, "Ultrase MT". Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Error Prevention staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

We first evaluated the appropriateness of the use of ‘MT’ in the name of this product. We considered how ‘MT’ may be interpreted. We also analyzed the potential for ‘MT’ to resemble any numbers, dosing instructions, or medical abbreviations, and considered comments concerning ‘MT’ from the Expert Panel in our analysis. The Division of Medication Error Prevention Expert Panel discussion noted that ‘MT’ is not a meaningful modifier. Representatives of the Division of Drug Marketing, Advertising, and Communications (DDMAC) agreed with this assessment. Furthermore, ‘MT’ could have multiple interpretations which were found using the handbook Medical Abbreviations and Dorland’s Illustrated Medical Dictionary. See Section 3.1.1 for details.

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

2.1.1.3 FDA Adverse Event Reporting System (AERS) Database

Since the Ultrase product line is currently in the marketplace, the FDA Adverse Event Reporting System (AERS) was searched for post-marketing safety reports related to “Ultrase MT”. The following criteria were used: MedDRA High Level Group Term (HLGT) “Medication Errors” and Preferred Term (PT), “Pharmaceutical Product Complaint” with the established name, trade name and verbatim letter string of “Ultra%” and “Pancrelip%”.

2.1.1.4 USP MEDMARx Database

A search was requested of the United States Pharmacopeia MEDMARx database for all Ultrase and Ultrase MT medication errors.

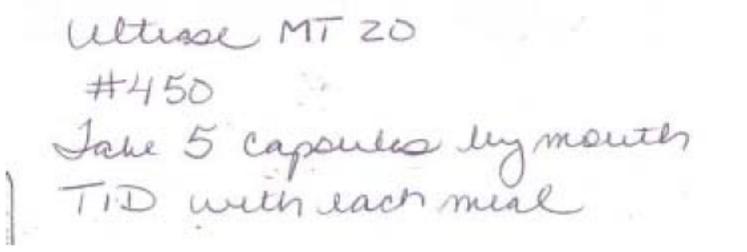
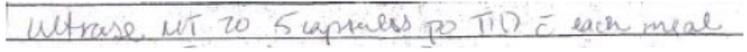
2.1.2 CDER Prescription analysis studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proprietary name, “Ultrase MT” 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 a total of 125 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of “Ultrase MT” in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 125 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to the medication error staff.

For the purpose of conducting the prescription studies, ‘Ultrase MT20’ was used as the proposed proprietary name.

Figure 1. “Ultrase MT” Prescription Study (conducted on December 5, 2007)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u></p>  <p>Ultrase MT 20 #450 Take 5 capsules by mouth TID with each meal</p>	<p>“Ultrase MT 20 #450 – 5 capsules by mouth TID with each meal”</p>
<p><u>Inpatient Medication Order :</u></p>  <p>Ultrase MT 20 5 capsules po TID c each meal</p>	

2.1.3 External Proprietary Name Risk Assessment

For this product, the Applicant submitted an independent risk assessment of the proposed proprietary name dated February 6, 2008 conducted by (b) (4) (b) (4) a consulting firm. We note that this external proprietary name risk assessment was submitted subsequent to the meeting held between the Division, the Applicant and the Division of Medication Error Prevention on January 16, 2008.

We conduct an independent analysis and evaluate data provided, and respond to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in the Division of Medication Error Prevention Staff’s database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator’s Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

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

2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying

where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike 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 Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking: “Is the name “Ultrase MT” convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?” An affirmative answer indicates a failure mode and represents a potential for “Ultrase MT” to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Division of Medication Error Prevention will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

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

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

2. The Division of Medication Error Prevention 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.©(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains a USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. 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 another drug product.

In the event that the Division of Medication Error Prevention objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, we will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while the medication error staff will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then the Division of Medication Error Prevention will not object to the use of the proprietary name. If any of these conditions are met, then we **will** object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, World Health Organization, Joint Commission of Accredited Healthcare Organizations, and Institute for Safe Medication Practices, have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the Division of Medication Error Prevention 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken 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 the approving the error-prone proprietary name. Moreover, even after Sponsor's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, the Division of Medication Error Prevention believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If the Division of Medication Error Prevention objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to

identify strategies to reduce the risk of medication errors. The Division of Medication Error Prevention is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for us to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container label and carton labeling communicates critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.⁷

Because the Division of Medication Error Prevention staff analyze reported misuse of drugs, we are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. The Division of Medication Error Prevention uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Sponsor submitted on July 31, 2007 and April 17, 2008 the following container labels and carton labeling for the Division of Medication Error Prevention to review (see Appendix F for images):

- Container Label
 - Ultrase MT12 (100 capsules)
 - Ultrase MT12 (Professional sample of 12 capsules)
 - Ultrase MT18 (100 capsules)
 - Ultrase MT20 (100 capsules and 500 capsules)
 - Ultrase MT20 (Professional sample of 12 capsules)
- Carton Labeling
 - Ultrase MT12 (Professional sample of 12 capsules)
 - Ultrase MT20 (Professional sample of 12 capsules)
- Package Insert Labeling : no image

⁷ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and information sources

Our search identified a total of eighteen (n=18) names as having some orthographic and/or phonetic similarity to the proposed proprietary name “Ultrase MT”. These names included Ultracet, Ultracef, Ultrasex, Ultram ER, Ultravate, Ultralente, Ultrasept, Ultravist, Vitrasert, Ultram, Ultiva, Ultane, Altace, Vitrase, Estrace, Ultragris-165, Ultragris-650 and Ultrase.

Ten (n=10) of the eighteen names were thought to look like “Ultrase MT”. These names included Ultrasex, Ultram, Ultram ER, Ultravate, Ultiva, Vitrase, Ultane, Ultrasept, Ultravist, and Vitrasert. Five (n=5) names (Ultracef, Ultragris-165, Ultragris-650, Ultralente, and Altace) were thought to sound like “Ultrase MT”. The remaining three (n=3) names (Estrace, Ultracet, and “Ultrase”) were thought to sound and look like “Ultrase MT”.

The Division of Medication Error Prevention staff noted that the letters ‘MT’ can stand for medical abbreviations or other terminologies: “empty”, “macular target”, “Maggott therapy”, “malaria therapy”, “maintenance therapy”, “malignant teratoma”, “masses of tenderness”, “Medical technologist”, “metatarsal”, “Medical Transcriptionist”, “methadone”, “middle turbinate”, “monitor technician”, “mucosal thickening”, “muscles and tendons”, “muscle tone”, “music therapy”, “myringotomy tube(s)”, “myringotomy with tu”, “magnetization transfer”, “mammary tumor”, “mammillothalamic tract” “manual traction”, “Many tailed Bandage (WWI Military Medical Term)”, “Martin Thayer”, “Mastoid Tip”, “Maximal Therapy”, “Mechanical Transport (WWI Military Medical Term)”, “Medial Thalamus”, “Medial Thickness”, “Medical Therapy”, “Meeting”, “Melatonin”, “Membrana Tympani”, “Mesangial Thickening”, “Metallothionein”, “Metatarsal”, “Methoxytryptamine”, “Methyltyrosine”, “Microtome”, “Microtubule”, “Mid Trachea”, “Minimal Touch”, “Missing Teeth”, “Monroe Tidal Drainage”, “More Than”, “Minimum Threshold”, “Motor Threshold”, “Movement Time”, “Muir Torre”, “Multiple Tics”, “Multitest”, and “Muscle Test”. However, the potential for confusion between these terms and “Ultrase MT” leading to medication errors is unlikely in the usual practice setting given the different context of use.

We note that the USAN stem for enzymes is ‘-ase’. The use of this stem in “Ultrase” is inconsistent with the USAN Council’s intent that stems be reserved for established names only.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by the Division of Medication Error Prevention staff (see section 3.1.1. above), and did not note any additional names thought to have orthographic or phonetic similarity to “Ultrase MT” and have the potential for confusion. It was noted that the proposed name was presented in the EPD agenda without the numerical modifiers, ‘12’, ‘18’, and ‘20’. However, it appears that this did not have an impact on the search strategies used to identify look-alike and/or sound-alike names.

DDMAC had no concerns regarding the proposed name from a promotional perspective, but there was concern from a safety perspective about what ‘MT’ stands for and that this suffix is not a common/standard trade name.

3.1.3 FDA Adverse Event Reporting System (AERS) Medication Error Cases

The AERS search yielded twelve (n=12) relevant medication error cases involving various pancrelipase products. These events span the time period from 2000 through 2007. Eight cases

involved the dispensing/administration of the wrong drug, three cases involved improper dose⁸ and the remaining case involved wrong strength. (See Appendix G for details). The types of errors are described below:

Wrong Drug (n=8)

- Four of the 8 cases involved Ultrase MT20 where substitution of a generic pancreatic enzyme drug for Ultrase MT 20 occurred due to an insurance requirement. The patients all complained of GI upset as a result of the substitution.
- The remaining four cases involved pancreatic enzyme substitutions or prescription misinterpretations leading to dispensing of other drugs.
 - One case involved dispensing Pacerone instead of pancrease. The patient outcome and contributing factors were not stated.
 - Two cases involved the substitution of one pancreatic enzyme for another. Details regarding why the substitution occurred and the contributing factors were not stated. In both cases patients complained of GI upset.
 - The remaining case concerned dispensing Ultram for Ultrase. Illegible handwriting was blamed for this medication error. The physician wrote ‘Ultrase 3 po tid cc’ and the ‘3’ was mistakenly interpreted as 3 – 50 mg tablets of Ultram. The patient received Ultram 150 mg orally three times daily for 2 days. Patient outcome was not stated.

Improper Dose (n=3)

In one case, Creon 10 was prescribed but Creon 10 capsules was entered in the computer. In another case Viokase 1 gram was dispensed and given to a patient but 0.1 g was prescribed. This patient recovered from cardiac arrest. In the remaining case, Viokase 8 was prescribed but the order was entered into the Medication Administration Record (MAR) as Viokase 8 tablets.

Wrong Strength (n=1)

In this case the patient received Creon 10 instead of Creon 20. The patient outcome and contributing factor was not stated.

3.1.4 USP MEDMARX*⁸ Medication Error Cases**

The United States Pharmacopeia searched the USP MEDMARX*** database for all Ultrase and Ultrase MT medication errors. This search yielded (b) (4) (n= (b) (4)) relevant cases of medication errors involving Ultrase or Ultrase MT products. These cases involved (b) (4) wrong drug cases, (b) (4) wrong strength cases and (b) (4) generic substitution cases. (See Appendix H for details). See below for a discussion of the types of errors.

Wrong Drug (n= (b) (4))

- In (b) (4), Ultrase was prescribed but (b) (4)
- In (b) (4) Ultrase was prescribed but (b) (4)

⁸ ** This document contains proprietary data from USP MEDMarx which cannot be shared outside of the FDA. Users wanting this information must contact Diane Cousins at USP (301) 816-8215. **

- In (b) (4), Ultrase was prescribed but (b) (4)

Wrong Strength (N=(b) (4))

- (b) (4) cases involved dispensing and/or administering of the wrong strength of the Ultrase MT product line. (b) (4)

Generic Substitution (N (b) (4))

- (b) (4) cases involved dispensing and/or administering of (b) (4)
- Conversely, in the remaining (b) (4) cases, a (b) (4)

3.1.5 CDER Prescription Analysis Studies

A total of 30 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. Over half of the participants (n=16) interpreted the name correctly as “Ultrase MT,” with correct interpretation occurring more frequently in the written studies. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the phonetic prescription study, with the proposed name, “Ultrase” reported as “Altrase” (n=5) or “Altrace” (n=1). These names sound similar to a currently marketed drug product, “Altace” which is an anti-hypertensive currently marketed in the U.S. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.6 External Name Studies

In the proposed name risk assessment submitted by the Sponsor, (b) (4) (b) (4) identified and evaluated a total of eleven drug names thought to have some potential for confusion with the name Ultrase MT.

Five of the eleven names were not previously identified in the Division of Medication Error Prevention Staff searches, the Expert Panel Discussion, or FDA prescription studies. These five (5) names (Activase, Kutrase, MCT Oil, Pancrease and Zomig-ZMT) identified by (b) (4) did not specifically list whether they share look-alike and/or sound-alike characteristics with “Ultrase MT”. These names were listed in the Computerized Orthographic and Phonologic Analysis (COPA).

3.1.7 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator identified no additional names thought to look similar to “Ultrase MT” and represent a potential source of drug name confusion. As such, a total of 23 names were analyzed to determine if the drug names could be confused with “Ultrase MT” and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and/or phonetic similarity to “Ultrase”, “Ultrase MT”, “Ultrase MT 12”, Ultrase MT18” or “Ultrase MT20” and thus determined to present some risk of confusion. Failure modes and effects analysis was then applied to determine if the proposed name, “Ultrase MT” could potentially be confused with any of the twenty-three (23) names and lead to medication error.

This analysis determined that the name similarity between “Ultrase”, “Ultrase MT”, “Ultrase MT 12”, Ultrase MT18” or “Ultrase MT20” and the identified names was unlikely to result in medication errors for twenty-one (21) of the twenty-three (23) products. For nineteen (19) names, FMEA determined that medication errors were unlikely because the products do not have a significant orthographic and/or phonetic similarity to “Ultrase MT” (Appendix C). One proprietary name, Ultrasept, was never approved by FDA and therefore confusion between Ultrasept and Ultrase MT is unlikely to occur in the usual practice setting. One product, Ultralente, FMEA determined that medication errors were unlikely because the product was withdrawn from the market (Appendix D).

The remaining two names, Altace and Ultrase, were vulnerable to confusion and medication errors due to orthographic and/or phonetic similarities in addition to overlapping product characteristics (see Section 4 below for details and Appendix E).

3.2 LABEL AND LABELING RISK ASSESSMENT

Review of the container labels, carton and package insert labeling identified several potential sources of medication error.

The Division of Medication Error Prevention notes that the draft carton and container labels submitted are in black and white and may not be a true representation of these items.

3.2.1 Container Label

The established name appears to be less than ½ the size of the proprietary name.

The strength of the product which is represented by the numerical modifier (e.g., 12) is not consistent with the actual amount of lipase units contained in a capsule.

The net quantity statement is stated in close proximity to the strength (i.e., list of contents per capsule).

The company name is more prominent than the drug name, strength and other product characteristics.

The dosage form is not clearly stated.

3.2.2 Package insert labeling

No comment.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

Our analysis of “Ultrase MT” determined it to be vulnerable to name confusion with Altace and within the Ultrase MT product line. Additionally, the use of letter abbreviations and numerical modifiers has resulted in misinterpretations leading to medication errors. We communicated these concerns to the Applicant on January 16, 2008. The Applicant responded to our concerns in correspondence dated February 10, 2008 and March 10, 2008. In response to the Applicant’s

correspondence we still maintain that the proposed name, “Ultrase MT” is vulnerable to name confusion for the following reasons:

4.1.1 Altace

Postmarketing data has identified cases of confusion between Altace and Ultrase because of their visual similarity to one another. Orthographically, the ‘U’ and ‘A’ may be difficult to distinguish from each other when the loop in the ‘A’ (for Altace) is not completely closed or when the ‘U’ (in Ultrase) is closed. Altace and Ultrase also share the letters ‘L’, ‘t’ and ‘e’ in the same positions in the name (ALTACE vs ULTRASE). Finally, this name pair sounds similar as ‘alt’ (in Altace) is not clearly distinguishable from ‘ult’ (in Ultrase) when spoken and the ‘c’ (in Altace) and ‘s’ (in Ultrase) have the same sound as well. It is also noted that in the prescription analysis studies, Ultrase MT was misinterpreted/mis spelled five (5) times for names beginning with ‘A’. Three responders believed the drug to be ‘Altrace MT’, one responder thought the drug to be ‘Altrace’ and the fifth responder believed the product to be ‘Altrase MT’. None of these names are available drugs. However, they are all close approximations of Altace.

Confusion has also occurred between Altace and Ultrase MT20 when the numerical modifier, ‘20’ has been misinterpreted as a strength or dose (as occurred in the two MedMARX*** reports cited earlier and in Appendix B). We anticipate continued confusion with this name pair if the modifier is kept as a number.

Altace
Ultrase

4.1.2 Ultrase

In correspondence dated February 14, 2008, the Applicant states that the marketing of Ultrase MS4 (also known as ‘Ultrase’ by frontline practitioners) (b) (4)

As a result, “Ultrase” will continue to exist along with “Ultrase MT” in the marketplace.

Confusion between this name pair, “Ultrase” and “Ultrase MT” may occur due to overlapping product characteristics such as indication of use, dosage forms, dosing frequency. This is the type of error frequently reported in product lines and this confusion may result in under-dosing or over-dosing increasing the potential for clinical instability or toxicity. In this case, ‘MT’ represents a higher amount of pancreatic enzymes contained within a minitab. Thus, if the prescriber omits the ‘MT’ portion of the name Ultrase will likely be dispensed although its dosage formulation differs from Ultrase MT. If that should occur in this case, the wrong drug would be dispensed which may result in inappropriate treatment and poor clinical control for the patient.

Additionally, Ultrase and the Ultrase MT products will likely be stored in close proximity to one another on a pharmacy or distributor/warehouse shelf. Typically, pharmaceutical products are organized alphabetically by proprietary name, established name, or sorted by manufacturer. Since these attributes are similar with Ultrase and the Ultrase MT products, it is likely that all four of these products will be stored near one another in virtually any organization carrying them. There is also a strong likelihood of label similarity between the products since they are from the same manufacturer. Thus, close storage proximity and similarity in label appearance may increase the risk of product selection errors. In order to minimize this potential source of

confusion, differentiation in the packaging and labeling of Ultrase, Ultrase MT 12, Ultrase MT 18, and Ultrase MT 20 is essential.

Another concern, due to the shared root of 'Ultrase', is the possibility for computer selection errors in which the wrong name and/or the wrong strength will be selected from a computer list of names beginning with the same character string. For example, Ultrase MT 12 will be selected when Ultrase MT 20 was intended or Ultrase MT 12, Ultrase MT 18 or Ultrase MT 20 will be selected when Ultrase was intended (or vice versa). Differentiation of labels and labeling will not be apparent during the computer entering process. Thus, education of practitioners will be extremely important so that they can make appropriate entries into their computer databases to differentiate these four names in their product menus to minimize computer selection errors.

4.1.3 Modifier

The use of letter abbreviations and numerical modifiers in a name is discouraged because they can be a source of confusion and may lead to medication errors because they may be ambiguous or unclear and result in misinterpretations. In this case, it appears that the letters 'MT' describe the technology used in the final dosage form. However, most practitioners would not know this and thus, it does not convey anything meaningful to the healthcare practitioner or consumer.

The numeric suffixes (12, 18 and 20) are added to the proprietary name to signify the lipase component in Ultrase MT. There are a number of problems that can arise from the use of numeric suffixes and suffixes in general. Specifically, it is common for modifiers/suffixes to be omitted from prescriptions or medications⁷, and for this product the use of numerical modifiers can be misinterpreted as the number of capsules to be taken. If the modifier is omitted with Ultrase MT, then the healthcare practitioner would have to contact the prescriber for clarification or simply dispense Ultrase MT. However, if the modifier is thought to be the number of capsules to be administered this could result in improper dosing or overdosing leading to adverse outcomes. Examples of such confusion include but are not limited to the following: Percocet 5, Viokase 8 and Creon 10. In all of these cases the number was misinterpreted as the number of tablets.

The numeric suffix can also cause problems when entering the prescription into the computer database as seen in this next example. The prescription order was written as Creon 10 cap 1 capsule QID. However, because of the way the order prints out once entered into the computer, the strength of 10 was confused as a dose of 10 capsules.

When the order printed on the medication administration record (MAR), the dose read: "10 CAP.EC."

~~Creon 10 cap 1 capsule QID~~

AMYL1CAP3 - CREON 10 CAPSULE EC 1 CAP.EC CAPSULE.DR

DOSE: 10 CAP.EC (10 CAPSULE.DRS PER DOSE)
ROUTE: PO
SIG: QID (SCH)
START: 09/ /06-1845 STOP: None SOFT:

computer entry

The reporter felt "the way the prescription was written could easily lead to errors and that the company's description of name and strength leads to confusion."

⁷ Lesar TS, Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8):579-587.

Because of these experiences and others with numerical modifiers that have been misinterpreted as dosage or days supply, we do not recommend their use. As stated in our previous review, the Division of Medication Error Prevention discourages the use of numerical modifiers that could be misinterpreted to mean a dose or a days' supply as a part of the proprietary name. This type of confusion could be averted if the names Ultrase MT12, Ultrase MT18, and Ultrase MT20 were revised to include the strength in terms of lipase such as Ultrase MT 13,800, Ultrase MT 20,700, and Ultrase MT 23,000.

4.2 THE DIVISION OF MEDICATION ERROR PREVENTION'S RESPONSE TO THE EXTERNAL NAME STUDY

The (b) (4) Proprietary Name Assessment favorably supports the continued use of Ultrase MT as a proprietary name. We find the methodology flawed and thus the conclusions have no to little evidence to support them. **First**, the assessment does not include the use of numerical modifiers. Although the name "Ultrase MT" is the proposed proprietary name, the numerical modifiers '12', '18' and '20' are used to differentiate between these products in the marketplace. Thus these names (Ultrase MT12, Ultrase MT18 and Ultrase MT20) are what the prescriber would use in providing an individualized dose for the patient. A prescription for "Ultrase MT" without the numerical modifiers would be meaningless to the pharmacist/nurse and therefore, assessment of "Ultrase MT" without its numerical modifiers does not represent real world experience.

Second, Altace was not found to look or sound like Ultrase because this name did not exceed COPA similarity thresholds and there have been no medication errors reported to the Applicant between these names, suggesting that they can and have safely co-existed since 1991. As indicated in the MEDMARX*** database, (b) (4)

(b) (4) See Appendix H for a description of the cases. The Division of Medication Error Prevention anticipates that, if the modifier is kept as a number, confusion about this name pair will continue. The orthographic and phonetic similarity between these two names in combination with their overlapping product characteristics such as strength and dose (Ultrase MT20 vs. Altace 20 mg) and route of administration create confusion. We further note that (b) (4) internal expert panel and survey of healthcare professionals, CDER prescription analysis studies and the expert panel for the Division of Medication Error Prevention all identified Altace as a sound-alike, look-alike name to Ultrase. The real world experiences of front line practitioners must be considered along with the orthographic and phonetic similarities and product characteristics between the proposed proprietary name and other marketed proprietary and established names. This identification of Altace as a look-alike, sound-alike name to Ultrase MT by different groups of healthcare practitioners is strong evidence of the potential for confusion between these two names. Thus, we believe that this name pair cannot safely coexist in the marketplace.

(b) (4) notes that the modifier MT has recognition among healthcare professionals who have used Ultrase MT. Other products such as Pancrease MT and Panocaps MT also exist in the marketplace. We note that these products are not approved by FDA and that these names were not reviewed by the Division of Medication Error Prevention. Furthermore, mere recognition of a modifier does not mean that confusion leading to medication errors has not and does not exist in the marketplace with these other products.

4.3 OVERLAPPING FORMULATIONS OF ULTRASE MT – OLD AND NEW

In correspondence dated January 4, 2008, the Applicant stated that "Axcen will continue to sell the remaining ULTRASE MT12, MT18 and MT20 that is in the pipeline and inventories." Therefore, there will be an overlap in the old and new formulations of Ultrase in the marketplace.

The Division of Medication Error Prevention notes that the lipase, protease and amylase components differ between the old and new formulations of Ultrase MT, however the numerical modifier remains unchanged leading the healthcare professional and the patient to believe they are receiving the same formulation as before. Along with the previously mentioned overlapping product characteristics, this change in formulation may result in medication errors as a result of lack of awareness in the healthcare community of the new product or the differences between Ultrase and the old and new formulations for Ultrase MT.

According to the Federal Register notice, manufacturers of pancreatic insufficiency products must have an approved NDA by April 28, 2008 in order to remain on the market. When the sponsor's NDA for the new formulation of Ultrase MT is approved, they do not plan on withdrawing the old formulation until April 28, 2008. This was confirmed via an email correspondence with the reviewing division's project manager. Thus, there will be a period of time in which both formulations would be available. This overlap of multiple formulations (old and new) of Ultrase MT could be confusing to healthcare practitioners. Additionally, if the name Ultrase MT is not revised as discussed in this review, we anticipate confusion leading to medication errors between the old and new formulations of Ultrase MT 12, Ultrase MT 18, and Ultrase MT 20. Our primary concern is that practitioners who are not aware of the introduction of the new strengths may assume the lipase content to be the same leading to unintentional overdoses. Additionally, they may not be aware that the amylase and protease units in the new formulation are different from the older versions making these different product formulations (see charts below). (*See Table 1, Section 1.3*)

4.4 USAN STEM

The proposed proprietary name, Ultrase, contains the USAN stem "-ase". USAN stems are intended to be reserved for established names only and therefore, the use of this name is inconsistent with the Council's intent. The goal of the USAN program is to provide meaningful, informative designations for compounds, enhancing correct prescribing practices and patient safety. The listing of USAN stems represents common stems for which chemical and/or pharmacologic parameters have been established. These stems and their definitions, approved by the USAN Council, are recommended for use in coining new nonproprietary names for drugs that belong to an established series of related agents. By adopting this system, similar compounds maintain a common "family" name that provides immediate recognition. Therefore, the Division of Medication Error Prevention does not recommend the use of Ultrase for this reason.

4.5 LABEL AND LABELING RISK ASSESSMENT

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed carton and container labels appears to be vulnerable to confusion that could lead to medication errors.

4.5.1 Product Strength

The strengths of the drug products are *not* consistent with the amount of the USP units of lipase per capsule which may cause confusion in the healthcare community. It would be ideal if the label stated the strength of the total lipase activity per capsule (e.g., 20,700 units).

4.5.2 Prominence of Information on Container Label and Carton Labeling

The net quantity is close in proximity to the content list per capsule. This proximity in numbers may lead to confusion because the net quantity and strengths overlap. This overlap may lead to selection errors and dispensing of the wrong strength.

Although the Applicant's name appears towards the bottom of the container label, it appears more prominent than other important information of its presentation in all capital and bolded letters. The most prominent information on the container label should be the proprietary name, established name, and product strength. Therefore, to increase the prominence of this information, the Applicant name should be minimized.

As currently presented, identification of the established name is difficult and the dosage form is not clearly stated. The established name should be at least half the size of the proprietary name and should be presented as (Pancrelipase) Capsule and located just below "Ultrase MT#" for ease of identification. "Enteric Coated Minitablets" is not the established name for this product and should not be presented as such.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Ultrase MT is vulnerable to name confusion with the trademarked name Altace and the parent drug Ultrase in addition to containing letter and numeric suffixes that could lead to medication errors. This finding was consistent with and supported by our prescription studies, by the Division of Medication Error Prevention's Expert Panel and in our post-marketing database search. As such, we object to the use of the proprietary name, Ultrase MT, and its numerical modifiers for this product. However, if **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product; the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed carton and container labels introduces vulnerability to confusion that could lead to medication errors. The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2.1 that aim at reducing the risk of medication errors.

5.1 COMMENTS TO THE DIVISION

Based upon our risk assessment of the proposed proprietary name, we object to the proposed proprietary name, Ultrase MT, for the reasons stated above.

We recommend that the comments in Section 5.2 be forwarded to the Applicant.

We would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention for any communication to the Applicant with regard to this review. If you have any questions or need clarification, contact Cheryle Milburne, Project Manager, at 301-796-2084.

5.2 COMMENTS TO THE APPLICANT

- A. The findings of our Proprietary Name Risk Assessment indicate that the proposed name, Ultrase MT, is vulnerable to name confusion that could lead to medication errors with Altace and the parent drug Ultrase, in addition to containing letter and numeric suffixes that could lead to medication errors. Our rationale is described in detail below. As such, the Division of Medication Error Prevention objects to the use of the proprietary name, Ultrase MT. We recommend you submit two alternate proprietary names and identify your primary and secondary choice.

Finally, we recommend the label recommendations outlined in Section 5.6 below be implemented to improve the prominence of the proprietary name, established name and dosage form as well as to clearly differentiate the net quantity from the contents per capsule. Further, the Division of Medication Error Prevention notes the strength is inconsistent with the number of units of lipase per capsule potentially increasing the risk of confusion leading to medication errors.

1. Altace

Postmarketing data has identified cases of confusion between Altace and Ultrase because of their visual similarity to one another. Orthographically, the 'U' and 'A' may be difficult to distinguish from each other when the loop in the 'A' (for Altace) is not completely closed or when the 'U' (in Ultrase) is closed. Altace and Ultrase also share the letters 'L', 't' and 'e' in the same positions in the name (ALTACE vs ULTRASE). Finally, this name pair sounds similar as 'alt' (in Altace) is not clearly distinguishable from 'ult' (in Ultrase) when spoken and the 'c' (in Altace) and 's' (in Ultrase) have the same sound as well. It is also noted that in the prescription analysis studies, Ultrase MT was misinterpreted/mis spelled five (5) times for names beginning with 'A'. Three responders believed the drug to be 'Altrace MT', one responder thought the drug to be 'Altrace' and the fifth responder believed the product to be 'Altrace MT'. None of these names are available drugs. However, they are all close approximations of Altace.

(b) (4)
(as occurred in the two MedMARX*** reports cited earlier and in Appendix B). We anticipate continued confusion with this name pair if the modifier is kept as a number.

Altace
Ultrase

2. Ultrase

In correspondence dated February 14, 2008, the Applicant states that the marketing of Ultrase MS4 (also known as 'Ultrase' by frontline practitioners) (b) (4)

(b) (4) As a result, "Ultrase" will continue to exist along with "Ultrase MT" in the marketplace.

Confusion between this name pair, "Ultrase" and "Ultrase MT" may occur due to overlapping product characteristics such as indication of use, dosage forms, dosing frequency. This is the type of error frequently reported in product lines and this confusion may result in under-dosing or

over-dosing increasing the potential for clinical instability or toxicity. In this case, 'MT' represents a higher amount of pancreatic enzymes contained within a minitab. Thus, if the prescriber omits the 'MT' portion of the name Ultrase will likely be dispensed although its dosage formulation differs from Ultrase MT. If that should occur in this case, the wrong drug would be dispensed which may result in inappropriate treatment and poor clinical control for the patient.

Additionally, Ultrase and the Ultrase MT products will likely be stored in close proximity to one another on a pharmacy or distributor/warehouse shelf. Typically, pharmaceutical products are organized alphabetically by proprietary name, established name, or sorted by manufacturer. Since these attributes are similar with Ultrase and the Ultrase MT products, it is likely that all four of these products will be stored near one another in virtually any organization carrying them. There is also a strong likelihood of label similarity between the products since they are from the same manufacturer. Thus, close storage proximity and similarity in label appearance may increase the risk of product selection errors. In order to minimize this potential source of confusion, differentiation in the packaging and labeling of Ultrase, Ultrase MT 12, Ultrase MT 18, and Ultrase MT 20 is essential.

Another concern, due to the shared root of 'Ultrase', is the possibility for computer selection errors in which the wrong name and/or the wrong strength will be selected from a computer list of names beginning with the same character string. For example, Ultrase MT 12 will be selected when Ultrase MT 20 was intended or Ultrase MT 12, Ultrase MT 18 or Ultrase MT 20 will be selected when Ultrase was intended (or vice versa). Differentiation of labels and labeling will not be apparent during the computer entering process. Thus, education of practitioners will be extremely important so that they can make appropriate entries into their computer databases to differentiate these four names in their product menus to minimize computer selection errors.

3. Modifier

The use of letter abbreviations and numerical modifiers in a name is discouraged because they can be a source of confusion and may lead to medication errors because they may be ambiguous or unclear and result in misinterpretations. In this case, it appears that the letters 'MT' describe the technology used in the final dosage form. However, most practitioners would not know this and thus, it does not convey anything meaningful to the healthcare practitioner or consumer.

The numeric suffixes (12, 18 and 20) are added to the proprietary name to signify the lipase component in Ultrase MT. There are a number of problems that can arise from the use of numeric suffixes and modifiers in general. Specifically, it is common for modifiers/suffixes to be omitted from prescriptions or medications¹⁰, and for this product the use of numerical modifiers can be misinterpreted as the number of capsules to be taken. If the modifier is omitted with Ultrase MT, then the healthcare practitioner would have to contact the prescriber for clarification or simply dispense Ultrase MT. However, if the modifier is thought to be the number of capsules to be administered this could result in improper dosing or overdosing leading to adverse outcomes. Examples of such confusion include but are not limited to the following: Percocet 5, Viokase 8 and Creon 10. In all of these cases the number was misinterpreted as the number of tablets.

The numeric suffix can also cause problems when entering the prescription into the computer database as seen in this next example. The prescription order was written as Creon 10 cap 1 capsule QID. However, because of the way the order prints out once entered into the computer,

⁷ Lesar TS, Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8):579-587.

the strength of 10 was confused as a dose of 10 capsules. When the order printed on the medication administration record (MAR), the dose read: "10 CAP.EC."

~~Creon 10 Cap 1 Capsule QID~~
AMYL1CAP3 - CREON 10 CAPSULE EC 1 CAP.EC CAPSULE.DR
DOSE: 10 CAP.EC (10 CAPSULE.DRS PER DOSE)
ROUTE: PO
SIG: QID (SCH)
START: 09/ /06-1845 STOP: None
SOFT: *compa ten entry*

The reporter felt "the way the prescription was written could easily lead to errors and that the company's description of name and strength leads to confusion."

Because of these experiences and others with numerical modifiers that have been misinterpreted as dosage or days supply, we do not recommend their use. As stated in our previous review, the Division of Medication Error Prevention discourages the use of numerical modifiers that could be misinterpreted to mean a dose or a days' supply as a part of the proprietary name. This type of confusion could be averted if the names Ultrase MT12, Ultrase MT18, and Ultrase MT20 were revised to include the strength in terms of lipase such as Ultrase MT 13,800, Ultrase MT 20,700, and Ultrase MT 23,000.

4. THE DIVISION OF MEDICATION ERROR PREVENTION'S RESPONSE TO THE EXTERNAL NAME STUDY

The ^{(b) (4)} Proprietary Name Assessment favorably supports the continued use of Ultrase MT as a proprietary name. We find the methodology flawed and thus the conclusions have no to little evidence to support them. **First**, the assessment does not include the use of numerical modifiers. Although the name "Ultrase MT" is the proposed proprietary name, the numerical modifiers '12', '18' and '20' are used to differentiate between these products in the marketplace. Thus these names (Ultrase MT12, Ultrase MT18 and Ultrase MT20) are what the prescriber would use in providing an individualized dose for the patient. A prescription for "Ultrase MT" without the numerical modifiers would be meaningless to the pharmacist/nurse and therefore, assessment of "Ultrase MT" without its numerical modifiers does not represent real world experience.

Second, Altace was not found to look or sound like Ultrase because this name did not exceed COPA similarity thresholds and there have been no medication errors reported to the Applicant between these names, suggesting that they can and have safely co-existed since 1991. As indicated in the MEDMARX*** database, ^{(b) (4)}

^{(b) (4)} See Appendix H for a description of the cases. The Division of Medication Error Prevention anticipates that, if the modifier is kept as a number, confusion about this name pair will continue. The orthographic and phonetic similarity between these two names in combination with their overlapping product characteristics such as strength and dose (Ultrase MT20 vs. Altace 20 mg) and route of administration create confusion. We further note that ^{(b) (4)} internal expert panel and survey of healthcare professionals, CDER prescription analysis studies and the expert panel for the Division of Medication Error Prevention all identified Altace as a sound-alike, look-alike name to Ultrase. The real world experiences of front line practitioners must be considered along with the orthographic and phonetic similarities and product characteristics between the proposed proprietary name and other marketed proprietary and established names. This identification of Altace as a look-alike, sound-alike name to Ultrase MT by different groups of healthcare practitioners is strong evidence of the potential

for confusion between these two names. Thus, we believe that this name pair cannot safely coexist in the marketplace.

(b) (4) notes that the modifier MT has recognition among healthcare professionals who have used Ultrase MT. Other products such as Pancrease MT and Panocaps MT also exist in the marketplace. We note that these products are not approved by FDA and that these names were not reviewed by the Division of Medication Error Prevention. Furthermore, mere recognition of a modifier does not mean that confusion leading to medication errors has not and does not exist in the marketplace with these other products.

5. OVERLAPPING FORMULATIONS OF ULTRASE MT – OLD AND NEW

In correspondence dated January 4, 2008, the Applicant stated that “Axcan will continue to sell the remaining ULTRASE MT12, MT18 and MT20 that is in the pipeline and inventories.” Therefore, there will be an overlap in the old and new formulations of Ultrase in the marketplace.

The Division of Medication Error Prevention notes that the lipase, protease and amylase components differ between the old and new formulations of Ultrase MT, however the numerical modifier remains unchanged leading the healthcare professional and the patient to believe they are receiving the same formulation as before. Along with the previously mentioned overlapping product characteristics, this change in formulation may result in medication errors as a result of lack of awareness in the healthcare community of the new product or the differences between Ultrase and the old and new formulations for Ultrase MT.

According to the Federal Register notice, manufacturers of pancreatic insufficiency products must have an approved NDA by April 28, 2008 in order to remain on the market. When the applicant’s NDA for the new formulation of Ultrase MT is approved, they do not plan on withdrawing the old formulation until April 28, 2008. This was confirmed via an email correspondence with the reviewing division’s project manager. Thus, there will be a period of time in which both formulations would be available. This overlap of multiple formulations (old and new) of Ultrase MT could be confusing to healthcare practitioners. Additionally, if the name Ultrase MT is not revised as discussed in this review, we anticipate confusion leading to medication errors between the old and new formulations of Ultrase MT 12, Ultrase MT 18, and Ultrase MT 20. Our primary concern is that practitioners who are not aware of the introduction of the new strengths may assume the lipase content to be the same leading to unintentional overdoses. Additionally, they may not be aware that the amylase and protease units in the new formulation are different from the older versions. (See Table 1, Section 1.3) In light of the potential for confusion if the old Ultrase MT formulation is co-marketed with the proposed formulation, the Division of Medication Error Prevention recommends that the older formulations be removed from the market once the new formulations are approved. If the sponsor is allowed to co-market both products, then we reiterate our concern that the sponsor not be allowed to use the numerical modifiers 12, 18 and 20 and that these products be named Ultrase MT 13,800, Ultrase MT 20,700, and Ultrase MT 23,000 to minimize confusion.

6. USAN STEM

The proposed proprietary name, Ultrase, contains the USAN stem “-ase”. USAN stems are intended to be reserved for established names only and therefore, the use of this name is inconsistent with the Council’s intent. The goal of the USAN program is to provide meaningful, informative designations for compounds, enhancing correct prescribing practices and patient safety. The listing of USAN stems represents common stems for which chemical and/or pharmacologic parameters have been established. These stems and their definitions, approved by

the USAN Council, are recommended for use in coining new nonproprietary names for drugs that belong to an established series of related agents. By adopting this system, similar compounds maintain a common "family" name that provides immediate recognition. Therefore, the Division of Medication Error Prevention does not recommend the use of Ultrase for this reason.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Sponsor to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

B. LABELS AND LABELING

1. As a general recommendation, on all of the labels and labeling, increase the prominence of the established name to at least ½ the size of the proprietary name in accordance with 21 CFR 201.10(g)(2).
2. As a general recommendation, on all of the labels and labeling, locate the established name in close proximity to the proprietary name along with the dosage form. Thus the established name would be "(Pancrelipase) Capsules" and located directly under "Ultrase MT". The description "enteric coated minitables" should be re-located away from this information to avoid confusion regarding the appropriate established name.

C. Container Label

1. Decrease the prominence of the company name such that it is less prominent and does not compete with other important information.
2. Relocate the net quantity away from the list of contents per capsule to avoid confusion.
3. The strength of the product is not consistent with the amount of the USP units of lipase. Furthermore, this inconsistency will be compounded by the availability of the new and old formulations in the marketplace. We recommend the proprietary name reflect the amount of lipase units per capsule. Thus, Ultrase MT12 would be named Ultrase 13,800 units, Ultrase MT18 would be named Ultrase 20,700 units, etc.

D. Insert Labeling

No comment.

6 REFERENCES

1. Adverse Events Reporting System (AERS)

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. Micromedex Integrated Index (<http://weblern/>)

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

3. Phonetic and Orthographic Computer Analysis (POCA)

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

4. Drug Facts and Comparisons, online version, St. Louis, MO (<http://weblern/>)

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

5. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

6. Division of Medication Errors and Technical Support proprietary name consultation requests

This is a list of proposed and pending names that is generated by DMETS from the Access database/tracking system.

7. 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](#) and [generic drugs](#) and [therapeutic biological products](#); [prescription](#) and [over-the-counter](#) human drugs and [therapeutic biologicals](#), [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

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

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

9. *WWW location* <http://www.uspto.gov>.

Provides information regarding patent and trademarks.

10. *Clinical Pharmacology Online* (<http://weblern/>)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. *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 tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. *Natural Medicines Comprehensive Databases* (<http://weblern/>)

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

13. *Stat!Ref* (<http://weblern/>)

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

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

List contains all the recognized USAN stems.

15. *Red Book Pharmacy's Fundamental Reference*

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

16. *Lexi-Comp* (www.pharmacist.com)

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

17. *Medical Abbreviations Book*

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendices may include the following:

- Standard description of databases
- Case series
- Detailed tables and charts with explanations
- Detailed problems, assumptions, constraints
- List of sponsor submissions
- Dissenting opinions

Appendix A:

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

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

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> • Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic	Similar spelling	<ul style="list-style-type: none"> • Names may look similar

	similarity	Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	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

Appendix B:

CDER Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Medication Order
Ultrase MT	Altrace MT	Ultrase MT
Ultrase MT	Altrace	Ultrase MT
Ultrase MT	Ultrase MT	Ultrase NT
Ultrase MT	Ultrase MT	Ultrase UT
Ultrase MT	Altrace MT	Ultrase MT
Ultrase MT	Altrace MT	Ultrase MT
Ultrase MT	Altrace MT	Ultrase MT

Ultrase MT	Ultrace MT	
ULTASE M	Ultrace MT	
Ultrase MT	Ultrace MT	
Ultrase MT	Ultrace MT	
	Altrace MT	

Appendix C: Names lacking convincing orthographic and/or phonetic similarity to “Ultrase MT”.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Ultrase MT12, Ultrase MT18, Ultrase MT20 (Pancrelipase Enteric Coated Minitablets)		Ultrase MT12, Ultrase MT18 and Ultrase MT20	Usual dose: 500 to 1,000 lipase USP units/kg/meal
Ultracet	Sound and Look	Acetaminophen 325 mg, tramadol 37.5 mg	Two tablets every 4 to 6 hours as needed
Ultram ER	Look	100 mg, 200 mg, 300 mg	One tablet daily (usually 100 mg initially)
Ultravate	Look	Halobetasol propionate cream 0.05%, Halobetasol propionate ointment 0.05%	Apply to affected area(s) twice daily
Ultravist	Look	311.70 mg iopromide and 150 mg iodine/mL; 498.72 mg iopromide and 240 mg iodine/mL; 623.4 mg iopromide and 300 mg iodine/mL; 768.86 mg iopromide and 370 mg iodine/mL	Individualized dosing that is administered one time

Vitrasert	Look	4.5 mg	Administer every 5 to 8 months
Ultracef	Sound	500 mg, 1 gm, 250 mg/5 mL, 500 mg/5 mL	1 g to 2 g in divided doses
Ultrasex	look	Three capsules contain: <u>Yohimbe</u> extract (4:1, equal to 1000 mg) 250 mg • <u>Avena Sativa</u> (wild oats) 200 mg • <u>Siberian Ginseng</u> 200 mg • <u>Damiana</u> 200 mg • <u>Saw Palmetto</u> 200 mg • <u>Sarsaparilla</u> 200 mg • <u>Fo-Ti</u> 100 mg • <u>Ginkgo Biloba</u> 50 mg • <u>Yerba Mate</u> 50 mg • <u>Irish Moss</u> 50 mg • White Yellow 50 mg • <u>Cayenne</u> 25 mg	Use as directed.
Ultiva	Look	1 mg, 2 mg, 5 mg powder for injection	Individualized to the Patient
Vitraxe	Look	6,200 units powder for injection; 200 units/mL solution for injection	One time administration
Ultane	Look	100% liquid for inhalation	Individualized to the Patient
Ultragris-165	Sound	165 mg oral tablet	500 mg to 1 g daily
Ultragris-330	Sound	330 mg oral tablet	500 mg to 1 g daily
Ultram	Look	50 mg oral tablet	50 mg to 100 mg every 4 to 6 hours
Activase	Look or Sound	50 mg and 100 mg powder for injection	100 mg as bolus or titrated continuous infusion
MCT Oil	Look or Sound	115 calories/15 mL	15 mL 3 to 4 times a day
Zomig ZMT	Look or Sound	2.5 mg, 5 mg oral tablet	Individualized to the patient not to exceed 10 mg/24 hours
Estrace	Look or sound	0.5 mg, 1 mg, 2 mg, 0.01%	1 mg to 2 mg three times daily titrated up to 10 mg three times daily; 2 grams to 4 grams daily for 1 to 2 weeks
Kutraxe	COPA	Lipase 2,400 units; protease 30,000 units; amylase 30,000 units	Take with meals and snacks based upon clinical symptoms of pancreatic enzyme deficiency
Pancrease	COPA	Pancrease MT4: lipase 4,000 units, protease 12,000 units, amylase 12,000 units; Pancrease MT10: lipase 10,000 units, protease 30,000 units, amylase 30,000 units; Pancrease MT16: lipase 16,000 units, protease 48,000 units, amylase 48,000 units; Protease MT20: lipase 20,000	Take with meals and snacks based upon clinical symptoms of pancreatic enzyme deficiency

		units, protease 44, 000 units, amylase 56,000 units	
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Appendix D: Products withdrawn from the market with no generic equivalent product available.

Proprietary Name	Similarity to Ultrase MT	Year product withdrawn by the sponsor
Ultralente	Sound alike	December, 2005

Appendix E: Names that look-alike and/or sound-alike “Ultrase MT”.

Ultrase MT12, Ultrase MT18, Ultrase MT20 (Pancrelipase Enteric Coated Minitablets)	Lipase/Amylase/Protease 13,800/27,600/27,600; 20,700/41,400/41,400; 23,000/46,000/46,000 Units of lipase per capsule	Usual dose: 500 to 1,000 lipase USP units/kg/meal
Failure Mode: Name confusion	Causes (could be multiple)	Effects
Altace	<p>Phonetic similarity to Ultrase secondary to rhyming quality of ‘Al-’ (ALtace) vs. ‘Ul-’ (ULtrase) and rhyming quality of ‘-tace’ (alTACE) vs ‘-trase’ (ulTRASE), both names have two syllables and the pronunciation of these names engages the same aspects of the mouth.</p> <p>Numerical overlap in strength and dose can occur when Altace dose is prescribed as 20 mg, potentially confused with Ultrase</p>	<p>Medication errors may occur as a result of confusion between Altace 20 mg and Ultrase MT20.</p> <p><i>Rationale: (why would this confusion occur?)</i></p> <p>The presence of a numerical modifier in the proposed name, Ultrase MT20 may lead the healthcare practitioner to identify the number with the quantity to dispense (or administer) or this numerical modifier may be confused with the intended strength of the product. Our safety concerns are evidenced by post-marketing surveillance which has shown that the use of ambiguous or unclear abbreviations have resulted in misinterpretations leading to medication errors. Additionally, because of the strong phonetic similarity between these two names, confusion may occur when there is verbal communication. Details regarding confusion between Altace and the proposed name, Ultrase is further discussed in Section 4.1.1.</p>

	MT20.	
Ultrase	<p>Orthographic similarity exists in the presence of the same root name ('Ultrase')</p> <p>Numerical overlap exists in the strengths of Ultrase and Ultrase MT which are both expressed as 'thousands of USP units' based upon the lipase content. See narrative for details.</p>	<p>Medication errors may occur as a result of confusion between Ultrase and Ultrase MT in the usual practice settings.</p> <p><i>Rationale:</i></p> <p>The root names for both "Ultrase" and "Ultrase MT" are the same. If the prescriber were to omit the modifier 'MT' from Ultrase, the patient would potentially receive a lower dose than prescribed causing a medication error. Confusion is further exacerbated by the expression of the amount of lipase for these two drug products. Both are prescribed as thousands of USP units based upon the lipase content and kilogram weight of the patient. Confusion could occur as a result of misinterpretation of the intended dose. See section XXXX for details.</p>

Appendix F: Carton and Container Labels

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Appendix G: AERS Medication Errors for ULTRASE MT

ISR#	Medication Error Type	Narrative	Patient outcome	Contributing factors
3716496-4	Wrong drug	Generic pancreatic enzymes substituted for Ultrase MT-20	GI upset	Insurance restrictions
3789254-2	Wrong drug	Dispensed Lipran UL20 instead of Ultrase 'UL-20'	Increased GI complaints, weight loss and increased pulmonary function test	Insurance restrictions
3765461-X	Wrong drug	Order written for Ultrase 3 po tid cc. Ultram 150 mg po tid as placed on patient's profile	Outcome not stated	Order written in felt tip pen and was very difficult to read
5171022-0	Wrong dose	Pharmacy received handwritten order for 'Creon 10 1 capsule QID'. Order entered into computer as 'Creon 10 capsules po QID'.	No patient harm	Pharmacist caught error before reaching patient
3863166-8	Wrong dose	Order received for 'Viokase 8 tabs with meals TID'. Correct order was 'Viokase-8 three tablets with meals TID'.	No patient harm	Pharmacist corrected order in MAR; Reporter stated clear confusion caused by use of the '8' suffix in the brand name
3468817-8	Wrong drug	Pacerone was dispensed instead of pancrease	Not stated	Not stated
4019553-0	Wrong drug	Patient normally takes Ultrase MT 20; substituted with generic pancreatic enzymes per Medicaid regulations	GI upset	Insurance restrictions
3975679-9	Wrong drug	Patient prescribed Ultrase MT 20 but dispensed generic enzyme according to Medicaid guidelines	GI upset	Insurance restrictions
4078102-1	Wrong strength	Prescription for Creon 20 was filled with Creon 10	Not stated	Not stated
5259586-X	Wrong dose	Viokase 1 gram dispensed instead of 0.1 gram	Cardiac arrest	No stated
4166223-4	Wrong drug	Patient received Pangestyme CN-20 instead of Lipram enzymes	GI upset	Not stated
3789255-4	Wrong drug	Patient received Lipram UL 20 instead of Creon 20	GI upset	Not stated

Appendix H. MedMARX* Data for Ultrase MT**

Record number #	product	Medication error type	Patient harm	comments
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/s/

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6/3/2008 06:29:15 PM
DRUG SAFETY OFFICE REVIEWER

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