

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**200796Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

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

Date: February 18, 2011

Application Type/Number: NDA 200796

Through: Todd Bridges, RPh, Team Leader  
Kellie Taylor, PharmD, MPH, Associate Director  
Division of Medication Error Prevention and Analysis (DMEPA)

From: Jibril Abdus-Samad, PharmD, Safety Evaluator  
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Edarbi (Azilsartan Medoxomil) Tablets  
40 mg and 80 mg

Applicant/Applicant: Takeda Pharmaceuticals North America

OSE RCM #: 2010-2229

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

## **1 INTRODUCTION**

This re-assessment of the proprietary name, Edarbi, responds to the anticipated approval of NDA 200796 within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Edarbi, acceptable in OSE Review 2010-1782, dated October 19, 2010. The Division of Cardiovascular and Renal Products (DCRP) noted no issues with the proposed name, Edarbi, during our initial review. Additionally, the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective on August 27, 2010.

## **2 METHODS**

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see Section 5) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the completion of the previous OSE proprietary name review. We use the same search criteria outlined in OSE Review #2010-1782, for the proposed proprietary name, Edarbi. Additionally, DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

## **3 RESULTS**

The safety evaluator searches of the databases listed in Section 5 identified an additional name, Adcirca, thought to look similar to Edarbi and represent a potential source of drug name confusion (see Appendix A). Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of February 17, 2011.

## **4 CONCLUSIONS AND RECOMMENDATIONS**

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

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

## 5 REFERENCES

1. Abdus-Samad, J. OSE Review #2010-1782: Proprietary Name Review for Edarbi. October 19, 2010.
2. **Drugs@FDA** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)  
Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.
3. **USAN Stems** (<http://www.ama-assn.org/ama/pub/category/4782.html>)  
USAN Stems List contains all the recognized USAN stems.
4. **Division of Medication Error Prevention and Analysis proprietary name requests**  
This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

**Appendix A:** Names with orthographic differences and/or different product characteristics that minimize the risk of medication error.

Product name with potential for confusion	Similarity to Edarbi	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
<p><b>Edarbi</b> (Azilsartan Medoxomil)</p>		<p><b>40 mg, 80 mg tablets</b></p>	<p><b>Take 1 tablet orally daily</b></p>	
<p>Adcirca (Tadalafil) for pulmonary arterial hypertension</p>	<p>Look</p>	<p>20 mg tablet</p>	<p>Take 40 mg (2 tablets) orally daily Overlapping Dose: 40 mg</p>	<p><b>Orthographic differences:</b> Edarbi contains an additional upstroke letter and dotted letter ('-bi') at the end of the name. Additionally, depending on how the letters 'E' and 'A' are scripted, they may be orthographically distinct.</p>

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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 19, 2010

Application Type/Number: NDA 200796

Through: Todd Bridges, RPh, Team Leader  
Denise Toyer, PharmD, Deputy Director  
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Division of Medication Error Prevention and Analysis  
(DMEPA)

From: Jibril Abdus-Samad, PharmD, Safety Evaluator  
Division of Medication Error Prevention and Analysis  
(DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Edarbi (Azilsartan Medoxomil) Tablets  
40 mg, 80 mg

Applicant/Applicant: Takeda Pharmaceuticals North America

OSE RCM #: 2010-1782

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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
3 RESULTS .....	5
3.1 Database and Information Sources.....	5
3.2 CDER Expert Panel Discussion .....	5
3.3 FDA Prescription Analysis Studies.....	6
3.4 Comments from the Division of Cardiovascular and Renal Products (DCRP) .....	6
3.5 Safety Evaluator Risk Assessment.....	6
4 DISCUSSION.....	6
4.1 Promotional Assessment .....	6
4.2 Safety Assessment.....	7
5 CONCLUSIONS AND RECOMMENDATIONS .....	7
5.1 Comments to the Applicant.....	7
6 REFERENCES .....	8
APPENDICES .....	10

## **EXECUTIVE SUMMARY**

This review summarizes DMEPA's evaluation of the proposed proprietary name, Edarbi for Azilsartan Medoxomil Tablets. Our evaluation identified no concerns from a safety and promotional perspective that would render the name unacceptable. Thus, DMEPA finds the proposed proprietary name, Edarbi, acceptable for this product. The Applicant will be notified by letter.

The proposed proprietary name must be re-evaluated 90 days prior to 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**

The Applicant, Takeda Pharmaceuticals North America, requested an assessment of the proposed proprietary name in a submission dated August 13, 2010. The Division of Medication Error Prevention and Analysis (DMEPA) assesses a proposed proprietary name regarding its potential for name confusion with other proprietary or established drug names in the usual practice settings. Additionally, DMEPA considers the Division of Drug Marketing, Advertising and Communications' (DDMAC's) promotional assessment of the name.

### **1.2 REGULATORY HISTORY**

The Applicant initially proposed the proprietary name, (b) (4), for this product. (b) (4) These concerns were communicated to the Applicant in a letter dated August 6, 2010. Subsequently, the Applicant submitted the proposed proprietary name, Edarbi, for review on August 13, 2010.

### **1.3 PRODUCT INFORMATION**

Edarbi is the proposed proprietary name for Azilsartan Medoxomil Tablets. Azilsartan Medoxomil Tablets is an Angiotensin II Receptor Blocker with a proposed indication of treatment of hypertension. The recommended starting dose in adults is 40 mg taken once daily. The dose may be increased to a maximum of 80 mg once daily when additional blood pressure reduction is required. If blood pressure is not controlled with Edarbi alone, additional blood pressure reduction can be achieved when Edarbi is co-administered with other antihypertensive agents, including diuretics. Edarbi will be available in 40 mg and 80 mg tablets in bottles of 30 and 90 tablets and 10 count blister packages. Physician samples will be available in a 7 count blister package. Edarbi should be stored at 25°C (77°F), with temperature excursions permitted to 15°-30°C (59°-86°F).

## **2 METHODS AND MATERIALS**

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

### **2.1 SEARCH CRITERIA**

For this review, particular consideration was given to drug names beginning with the letter ‘E’ 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.<sup>1,2</sup>

To identify drug names that may look similar to Edarbi, the DMEPA safety evaluators also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (three, capital letter E, lowercase d, lowercase b), down strokes (none), cross strokes (none), and dotted letters (one, i). Additionally, several letters in Edarbi may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Edarbi.

When searching to identify potential names that may sound similar to Edarbi, the DMEPA safety evaluators search for names with similar number of syllables (three), stresses (e-DAR-bi or E-dar-bi), and placement of vowel and consonant sounds. The Applicant’s intended pronunciation (eh-DAR-bee) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

### **2.2 FDA PRESCRIPTION ANALYSIS STUDIES**

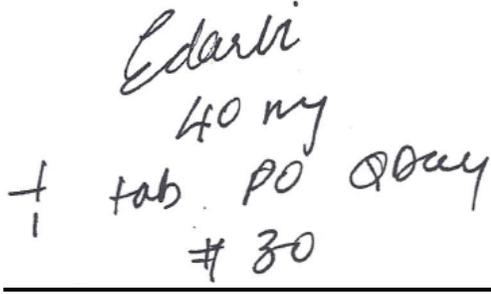
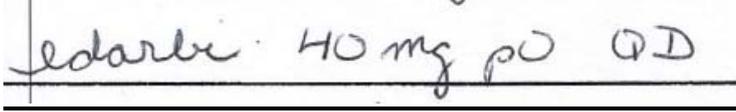
In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following outpatient medication order, inpatient medication order and verbal prescription were communicated during the FDA prescription studies.

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

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

**Figure 1. Edarbi Prescription Study (conducted on September 8, 2010)**

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Medication Order:</u></p>  <p>Edarbi 40 mg + 1 tab po QDay # 30</p>	<p>Edarbi 40 mg Take 1 daily</p>
<p><u>Inpatient Medication Order:</u></p>  <p>edarbi 40 mg po QD</p>	

### 3 RESULTS

The names identified from DMEPA’s methods as potential sources for name confusion with Edarbi are listed below.

#### 3.1 DATABASE AND INFORMATION SOURCES

Our searches of database and DMEPA’ information sources yielded a total of 14 names as having some similarity to the name Edarbi.

Twelve of the names were thought to look like Edarbi. These include: Chantix, Ebrex 600, Edluar, Efasin, Eleaf, Embeda, Enbrel, Endodan, Epivir, Etrafon, Evista, and Idarac. The two remaining names, Darbid<sup>\*\*\*</sup> and Edarbi, were thought to look and sound similar to Edarbi.

Additionally, DMEPA safety evaluators did not identify any United States Adopted Names stems in the proposed proprietary name, as of September 28, 2010.

#### 3.2 CDER EXPERT PANEL DISCUSSION

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

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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 42 practitioners responded to the prescription analysis study. Six of the responses in the Outpatient Study were correct. The most common misinterpretation in this study was the lowercase letter 'l' for the lowercase letter 'b'. Nine of the Inpatient Study responses were correct. The majority of the Verbal Study responses were incorrect with most common misinterpretation was the 'y' for the letter 'i'. None of the responses were similar to any currently marketed product.

### **3.4 COMMENTS FROM THE DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS (DCRP)**

#### ***3.4.1 Initial Phase of Review***

In response to an August 30, 2010, OSE e-mail, the Division of Cardiovascular and Renal Products (DCRP) indicated they had no issues at the initial phase of the name review.

#### ***3.4.2 Midpoint of Review***

DMEPA notified DCRP via e-mail that we had no concerns with the proposed proprietary name, Edarbi, on October 7, 2010. Per e-mail correspondence from DCRP on October 12, 2010, they noted no issues with the proposed proprietary name, Edarbi.

### **3.5 SAFETY EVALUATOR RISK ASSESSMENT**

Independent searches by the primary DMEPA safety evaluator resulted in the identification of 12 additional names which were thought to look or sound similar to Edarbi and represent a potential source of drug name confusion. Eleven names (Aclasta<sup>\*\*\*</sup>, Aldara, Aclovate, (b) (4)<sup>\*\*\*</sup>, Elavil, Elidel, (b) (4)<sup>\*\*\*</sup>, (b) (4)<sup>\*\*\*</sup>, Idarubicin, (b) (4)<sup>\*\*\*</sup>, and Inderal) were identified as having look-alike similarities. The remaining name, (b) (4)<sup>\*\*\*</sup>, was thought to have sound-alike similarities.

Thus, we identified in total, 26 names as having similarity to the proposed name.

## **4 DISCUSSION**

This proposed name, Edarbi, was evaluated from a safety and promotional perspective. Furthermore, input from pertinent disciplines involved with the review of this application was considered accordingly.

### **4.1 PROMOTIONAL ASSESSMENT**

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

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<sup>\*\*\*</sup> This document contains proprietary and confidential information that should not be released to the public.  
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## **4.2 SAFETY ASSESSMENT**

DMEPA identified 26 names for their potential similarity to the proposed name, Edarbi. No other aspects of the name were determined to pose a different source for potential confusion with the name.

Twelve of the 26 names were eliminated for the reasons described in Appendices D through F. Appendix D lists four proprietary name which lacks sufficient orthographic similarity with Edarbi to result in confusion. Appendix E describes a proprietary name of a foreign product. Appendix F describes seven proprietary names for products that are inactive. Additionally, the name, Edarbi, was identified in our database search and is actually the name for this product under review. Since the trademark is licensed to the Applicant, it was eliminated from further analysis.

Failure mode and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the remaining 13 names and lead to medication errors. This analysis determined that the name similarity between Edarbi and all of the 13 identified names was unlikely to result in medication error for the reasons presented in Appendix G.

## **5 CONCLUSIONS AND RECOMMENDATIONS**

We have completed our review of the proposed proprietary name, Edarbi, and it is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis has no objections to the proprietary name, Edarbi, at this time. The Applicant will be notified via letter.

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.

If you have further questions or need clarifications, please contact Nina Ton, project manager, at 301-796-1648.

### **5.1 COMMENTS TO THE APPLICANT**

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

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

If any of the proposed product characteristics as stated in your August 13, 2010, submission are altered, the proprietary name should be resubmitted for review.

## 6 REFERENCES

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

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

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

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

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

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

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

DARRTS is a government database used to organize Applicant and Applicant 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](http://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](http://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](http://www.naturaldatabase.com))**

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

**12. Stat!Ref ([www.statref.com](http://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.

**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](http://www.lexi.com))**

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

**16. Medical Abbreviations Book**

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

## APPENDICES

### **Appendix A:**

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, NDA, 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.<sup>3</sup>

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.<sup>4</sup> 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.

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

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

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.<sup>5</sup> DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

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

## **1. Database and Information Sources**

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

## **2. CDER Expert Panel Discussion**

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

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

## **3. FDA Prescription Analysis Studies**

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

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

#### **4. Comments from the OND review Division or Generic drugs**

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

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

#### **5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>6</sup> 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?”***

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

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

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

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

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

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

- 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, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

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

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.

**Appendix B:** Potential orthographic or phonetic misinterpretation of the letters in the name Edarbi

Letters in Name, Edarbi	Scripted may appear as	Spoken may be interpreted as
Capital 'E'	F	any vowel
lowercase 'e'	a, c, i, l	any vowel
lowercase 'd'	cl, l	t
lowercase 'a'	ci, ce, e, o, u	any vowel
lowercase 'r'	c, n, v	wr
lowercase 'b'	l, li	p, v
lowercase 'i'	e,	any vowel

**Appendix C: FDA Prescription Study Responses (September 8, 2010)**

<b>Outpatient Medication Order</b>	<b>Inpatient Medication Order</b>	<b>Voice Prescription</b>
Edarbi	Edarbi	Darby
Edarbi	edarbi	Darby
Edarbi	Edarbi	Darvy
Edarbi	Edarbi	Edarbee
Edarbi	Edarbi	Edarbi
Edarbi	Edarbi	Edarbi
Edarir	edarbi	Edarby
Edarir	Edarbi	Edarby
Edarir	Edarbi	Edarby
Edarli	Edarir	Edarby
Edarli	Edarli	Edarby
Edarli	Idarbe	Edarby
Edarli	Idarbi	Edarvy
Edarlr	Idarbi	
endarbi		

**Appendix D: Proprietary Name lacking significant orthographic similarities**

<b>Proprietary Name</b>	<b>Similarity to Edarbi</b>	<b>Source</b>
Ebrex 600	Look	EPD
Efasin	Look	EPD
Epivir	Look	EPD
Evista	Look	EPD

**Appendix E:** Proprietary name of foreign product

Proprietary Name	Similarity to Edarbi	Comments
Idarac (Floctafenine)	Look	Name of product in foreign countries

**Appendix F:** Proprietary names no longer active

Proprietary Name	Similarity to Edarbi	Comments
Aclasta <sup>***</sup> (Zoledronic Acid)	Look	(b) (4)
(b) (4)	(b) (4)	(b) (4)
Darbid <sup>***</sup> (Isopropamide Iodide)	Look / Sound	(b) (4)

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

**Appendix G:** Names with orthographic differences and/or different product characteristics that minimize the risk of medication error.

Product name with potential for confusion	Similarity to Edarbi	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
<b>Edarbi</b> (Azilsartan Medoxomil)		<b>40 mg, 80 mg tablets</b>	<b>Take 1 tablet orally daily</b>	
Chantix (Varenicline Tartrate)	Look	0.5 mg, 1 mg, tablet	Days 1 to 3: Take 0.5 mg once daily  Days 4 through 7: Take 0.5 mg 2 times daily  Days 8 through end of treatment:  Take 1 mg 2 times daily	<b>Orthographic differences:</b> Chantix contains 2 crosstroke letter ('t', 'x')  <b>Dose:</b> 0.5 mg or 1 mg vs. 40 mg, 80 mg
		Starting Month Pack	Take as directed	A prescription for Starting Pack must contain the word 'Starting' to differentiate from the Continuing Pack. Additionally, the prescription may also read "Use as directed".  A prescription for Edarbi must contain the intended strength.
		Continuing Month Pak	Take as directed	A prescription for Continuing Pack must contain the word 'Continuing' to differentiate from the Starting Pack. Additionally, the prescription may also read "Use as directed".  A prescription for Edarbi must contain the intended strength.
Edluar (Zolpidem Tartrate)	Look	5 mg, 10 mg sublingual tablets	Take 1 tablets under the tongue at bedtime	<b>Dose:</b> 5 mg, 10 mg vs. 40 mg, 80 mg  <b>Route of administration:</b> sublingual vs. oral  A prescription for Edluar may contain instructions for sublingual administration and bedtime administration.
Eleaf (Avobenzone, Octinoxate, Octocrylene, Oxybenzone and Zinc Oxide)	Look	SPF 30 cream	Apply prior to sun exposure	<b>Dosage form and route of administration:</b> topical cream vs. oral tablets  A prescription for Edarbi must contain the intended strength.

Product name with potential for confusion	Similarity to Edarbi	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
<b>Edarbi (Azilsartan Medoxomil)</b>		<b>40 mg, 80 mg tablets</b>	<b>Take 1 tablet orally daily</b>	
Embeda (Morphine sulfate and Naltrexone Hydrochloride )	Look	30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, 100 mg/4 mg extended release capsules	Take tablet orally 2 times daily	<b>Orthographic Differences:</b> The first two upstrokes letters in Embeda are separated by the letter 'm'.  <b>Dose:</b> 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, 100 mg/4 mg vs. 40 mg, 80 mg  <b>Frequency of Administration:</b> 2 times daily vs. once daily  For confusion occur between this name pair, there must be orthographic confusion, omission of the Naltrexone component of the Embeda 80 mg/3.2 mg
Enbrel (Etanercept)	Look	25mg/0.5 mL, 50 mg/mL injection 25 mg kit 50 mg/mL injection 4(Sure Click)	Ankylosing Spondylitis, Psoriatic Arthritis, and Rheumatoid Arthritis: Inject 50 mg subcutaneously every week  Plaque Psoriasis: Inject 50 mg subcutaneously 2 times weekly x 3 months, then reduce to 50 mg weekly  Children Juvenile idiopathic Arthritis: 0.8 mg/kg subcutaneous weekly	<b>Dose:</b> 50 mg vs. 40 mg, 80 mg  <b>Dosage form and route of administration:</b> subcutaneous injection vs. oral tablets  <b>Frequency of Administration:</b> 1 to 2 times weekly vs. once daily
Endodan (Oxycodone and Aspirin)	Look	5 mg/325 mg tablets	Take 1 tablet every 6 hours as needed for pain; maximum dose aspirin 4 g/day	<b>Orthographic Differences:</b> The first two upstrokes letters in Endodan are separated by the letter 'n' and Endodan has two letters ('a', 'n') after the last upstroke letter 'd'.  <b>Dose:</b> 5 mg/325 mg vs. 40 mg, 80 mg  <b>Frequency of Administration:</b> 2 to 3 times daily as needed vs. once daily

Product name with potential for confusion	Similarity to Edarbi	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
<b>Edarbi (Azilsartan Medoxomil)</b>		<b>40 mg, 80 mg tablets</b>	<b>Take 1 tablet orally daily</b>	
Etrafon (Perphenazine Hydrochloride, Amitriptyline)  discontinued product, generics available	Look	2 mg/10 mg, 2 mg/25 mg tablets	Take 1 tablet orally 2 times daily	<b>Dose:</b> 2 mg/10 mg, 2 mg/25 mg vs. 40 mg, 80 mg <b>Frequency of Administration:</b> 2 to 4 times daily vs. once daily  Maximum recommended dose Perphenazine 4 mg daily
Aldara (Imiquimod)	Look	5% cream	Actinic Keratosis: Apply to affected area 2 times per week, prior to bedtime  Genital and Perianal warts: Apply a thin layer to affected area 3 times per week at bedtime	<b>Dosage form and route of administration:</b> topical cream vs. oral tablets <b>Frequency of Administration:</b> 2 to 3 times weekly vs. once daily  A prescription for Edarbi must contain the intended strength
Aclovate (Alclometasone Dipropionate)	Look	0.5 % cream, ointment	Apply to affected area 2 to 3 times daily	<b>Dosage form and route of administration:</b> topical cream vs. oral tablets <b>Frequency of Administration:</b> 2 to 3 times daily vs. once daily  A prescription for Edarbi must contain the intended strength
Elavil (Amitriptyline Hydrochloride)	Look	10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg	Take 1 tablet orally 1 to 3 times daily	<b>Orthographic Differences:</b> Elavil contains 3 letters ('-avi-') while Edarbi contains 2 letters ('-ar-') between the 2 <sup>nd</sup> and 3 <sup>rd</sup> upstrokes letters. Edarbi contains a dotted letter (i) after the least upstroke letter 'b') <b>Dose:</b> 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg vs. 40 mg, 80 mg  It is unlikely that a healthcare provider will prescribe Elavil 40 mg or 80 mg when readily available strengths of Elavil 50 mg and 75 mg are available.

Product name with potential for confusion	Similarity to Edarbi	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
<b>Edarbi (Azilsartan Medoxomil)</b>		<b>40 mg, 80 mg tablets</b>	<b>Take 1 tablet orally daily</b>	
Elidel (Pimecrolimus)	Look	1% cream	Apply to affected area 2 times daily	<b>Dosage form and route of administration:</b> topical cream vs. oral tablets  <b>Frequency of Administration:</b> 2 times daily vs. once daily  A prescription for Edarbi must contain the intended strength
Idarubicin	Look	5 mg/5 mL, 10 mg/10 mL, 20 mg/20 mL injection	Inject 12 mg/m <sup>2</sup> daily for 3 days by slow IV injection over 10 to 15 minutes	<b>Orthographic Differences:</b> Idarubicin is longer name (10 letters vs. 6 letters)  <b>Dose:</b> 20 mg (BSA 1.73 m <sup>2</sup> ) vs. 40 mg, 80 mg  <b>Dosage form and route of administration:</b> slow intravenous injection vs. oral tablets
Inderal (Propranolol Hydrochloride)	Look	20 mg, 40 mg, 60 mg, 80 mg tablets  (10 mg, 20 mg, 40 mg, 60 mg, 80 mg available in generic form)	Take 1 to 3 tablets orally 2 times daily (Dose range: 40 mg to 320 mg per day)	<b>Orthographic Differences:</b> Capital letters 'E' and 'I' are not orthographically similar, thus the letter must be lowercase for orthographic similarity. Inderal contains a letter 'n' between the 1 <sup>st</sup> and 2 <sup>nd</sup> upstroke letters. Edarbi contains a dotted letter ('i') after the last upstroke letter.  A prescription for Inderal oral solution will contain words such as mL, teaspoonful, or solution to distinguish it from a prescription for the oral tablet
		20 mg/5 mL, 40 mg/5 mL oral solution	Take 2.5 mL to 10 mL orally 2 times daily	

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/s/

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