CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-250s000

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:	December 17, 2009
To:	Russell Katz, MD Director, Division of Neurology Products (DNP)
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):	Ampyra (Dalfampridine) Extended-release Tablets 10 mg
Application Type/Number:	NDA# 022250
Applicant:	Acorda Therapeutics, Inc.
OSE RCM #:	2009-2258

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

CONTENTS

EXECUTIVE SUMMARY

Ampyra is the proposed proprietary name for Dalfampridine Extended-release Tablets. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns with the proposed proprietary name that would render the name unacceptable based on potentially similar names. However, we identified vulnerability with the proposed established name that could lead to name confusion. Initially, the Applicant submitted the established name, fampridine, which was considered to be similar to famotidine. These concerns were discussed with the Division of Neurology Products and the Applicant and the Division requested the Applicant revise their established name prior to approval. The new established name is dalfampridine. Thus, DMEPA evaluated the proprietary name, Ampyra with the new established name dalfampridine. Our re-review finds the proposed proprietary name, Ampyra, acceptable for this product. This is considered to be a final review.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Acorda Therapeutics on November 20, 2009, for an assessment of the proposed proprietary name, Ampyra, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

1.2 REGULATORY HISTORY

The proposed proprietary name, (b) (4) was found to be acceptable by DMEPA August 3, 2009, (OSE# 2009-938). (b) (4) As a result, the Applicant submitted an alternative name, Ampriva. DMEPA objected to this name November 24, 2009 (OSE# 2009-1763) due to its orthographic and phonetic similarities to the marketed name, Emtriva, as well as overlapping product characteristics shared by this name pair. Therefore, the Applicant withdrew from consideration the proposed name, Ampriva and submitted an alternative name, Ampyra.

1.3 PRODUCT INFORMATION

Ampyra (dalfampridine) is indicated for the treatment of patients with multiple sclerosis for the improvement of walking ability. The recommended dose is 10 mg twice daily approximately 12 hours apart with or without food. Clinical studies indicate that doses greater than 10 mg twice daily do not confer additional benefit and may increase the risk of adverse events. Ampyra will be supplied as a 10 mg non-scored tablet in 60-count bottles. Tablets should be taken whole and not divided, crushed, chewed or dissolved.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'A' 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 Ampyra, 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 (6 letters), upstrokes (1, capital letter 'A'), down strokes (two, p and y), cross-strokes (none), and dotted letters (none). Additionally, several letters in Ampyra 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 Ampyra.

When searching to identify potential names that may sound similar to Ampyra, the DMEPA staff search for names with similar number of syllables (3), stresses (am-PY-ra or AM-py-ra, am-py-RA), 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.

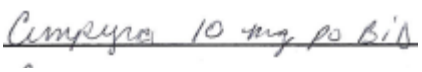
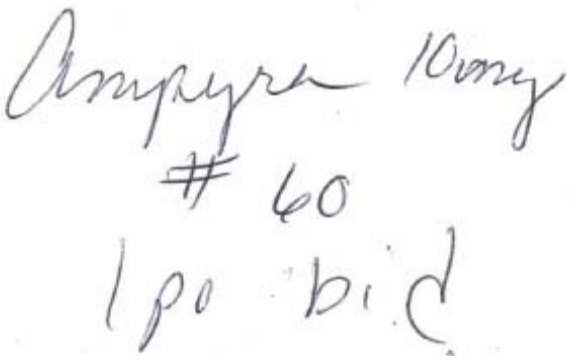
2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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 prescription was 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. Ampyra Prescription Study (conducted on November 30, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	"Ampyra 10 mg # 60 – take 1 tab po BID"
Outpatient Prescription: 	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

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

Twenty of the names were thought to look like Ampyra. These include Acanya, Agrylin, Amaryl, Amdry-C, Amdry-D, (b) (4), Campral, Cimzia, Compro, Inspra, (b) (4), (b) (4), Onglyza, Onrigin, Reopro, Semprex-D, Spiriva, and (b) (4). Two of the names (Alkeran and Apidra) were thought to sound like Amprya. The remaining six names were thought to look and sound similar to Ampyra: Amaya***, Ampriva***, Ampyra, Ampyrox, Antara, and (b) (4).

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of December 4, 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 Ampyra.

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-four practitioners responded but none of the responses overlapped with any existing or proposed drug names. Seven of the participants interpreted the name correctly as "Ampyra," with correct interpretation occurring in the outpatient written study (n= 5), the inpatient written study (n = 1) and the verbal study (n=1). The remainder of the responses misinterpreted the drug name. In the inpatient study, eleven of twelve practitioners misinterpreted the name. The first letter ('A') was misinterpreted as the combination letters 'Ce-' or 'Ci-'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 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 Ampyra and represent a potential source of drug name confusion.

Two names that were identified in our searches were Amaya*** and Ampriva ***. Amaya *** was the proposed proprietary name submitted by the Applicant previously (See Section 1.2 Regulatory History) and Ampyra *** is the subject of this review. Additionally, the name 'Ampyrox' was found to be the same name as [redacted] (b) (4). Therefore, these names (Amaya ***, Ampriva ***, Ampyra and Ampyrox) were not evaluated further. As such, twenty-four names were evaluated for their potential similarity to the proposed name, Ampyra.

3.5 COMMENTS FROM THE DIVISION OF NEUROLOGY PRODUCTS (DNP)

3.5.1 Initial Phase of Review

In response to an e-mail from OSE dated November 25, 2009, the Division of Neurology Products communicated that they concurred with DDMAC's acceptability of the trade name, Ampyra at the initial phase of the name review. They did not offer any other comment on the name.

3.5.2 DMEPA Mid-Point Review

DMEPA notified the Division of Neurology Products via e-mail that we had no objections to the proposed proprietary name, Ampyra, on December 14, 2009. Per e-mail correspondence from the Division of Neurology Products on December 14, 2009, they indicated they concur with our assessment of the proposed proprietary name, Ampyra**.**

4 DISCUSSION

DDMAC and the Division of Neurology Products have no concerns with this name. Additionally, DMEPA did not identify any factors associated with the proposed name other than names that potentially sound and look similar to Ampyra that would render the name unacceptable at this time.

Twenty-four names were identified and evaluated for their potential similarity to the proposed name, Ampyra. Five of the twenty-four names lacked orthographic and/or phonetic similarity and thus 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 nineteen names and lead to medication errors. This analysis determined that the name similarity between Ampyra and the remaining nineteen products was unlikely to result in medication errors for the reasons presented in Appendices E through G.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Ampyra, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. However, the proposed established name, fampridine, was considered to be similar to famotidine (the established name for Pepcid). After discussion with the Division, the Applicant was contacted to recommend revision of their established name prior to approval. As a result, the new established name was revised to dalfampridine.

Since the revised established name represents a change in product characteristics, DMEPA re-evaluated the proprietary name, Ampyra. Our re-review finds the proposed proprietary name, Ampyra, acceptable for this product. This is considered to be a final review.

If you have further questions or need clarifications, please contact Laurie Kelley, OSE project manager, at 301-796- 5068.

5.1 COMMENTS TO THE APPLICANT

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

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. AMF Decision Support System [DSS]

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

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

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 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.

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

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[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.

because similarly in 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	• 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	• 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, 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 posses 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:

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

"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 (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, Ampyra	Scripted may appear as	Spoken may be interpreted as
Capital 'A'	O, Q, Ci-, or Ce-	any vowel
lower case 'm'	n, z	'n'
lower case 'p'	q, g, y	
lower case 'y'	g, j, p	'i' or 'eye'
lower case 'r'	v, n	
lower case 'a'	e,c,	Any vowel

Appendix C: **FDA Prescription Study Responses for Ampyra**

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Cempyra	Anipyra	Ampira
Cimpyra	Ampyra	Ampyra
Cimpyra	Ampyra	Empira
Cimpyra	Ampyra	Empira
Cimpyra	Anipyra	Ampira
Cempyra (or maybe Cimpyra	Ampyra	
Cimpyra	Ampyra	
Cimpyra		
Cempyra		
Cimpyra		
Cimpyra		
Ampyra		

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

Name	Similarity to Amprya
(b) (4)	Look and Sound
Semprex-D	Look
Antara	Look and Sound
Alkeran	Sound
Reopro	Look

Appendix E: Unapproved Proprietary Name.

Proprietary Name	Similarity to Ampyra	Comments
(b) (4)	Look	(b) (4)

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

Appendix F: Names which have limited product characteristic information.

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

Appendix G: Potential confusing name which is unlikely to cause medication errors.

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale that minmizes the risk of the failure mode to occur**
Proprietary Name	**Strength**	**Usual Dose:**
Ampyra	**10 mg tablet**	**10 mg orally twice daily**
Amaryl (glimepiride) Tablet 1 mg, 2 mg, 4 mg	Orthographic similarity stems from sharing the same letters (A, M, R AND Y). Numerical overlap in strength exists (1 mg vs. 10 mg) These names share the same route of administration (oral). Potential for same frequency (twice daily) although Amaryl is recommended for once daily administration.	The presence of the upstroke ('l') at the end of Amaryl distinguishes this name from Ampyra when scripted. Additionally, Amaryl contains a down-stroke followed by an upstroke at the end of the name vs. two sequential down-strokes in the name, Ampyra. These differences should minimize confusion between this name pair. Several factors would have to occur simultaneously to facilitate a medication error. If a physician prescribed Ampyra 10 mg orally twice daily and the pharmacist/nurse misinterpreted the name as Amaryl, the total daily dose would be 20 mg which greatly exceeds the 8 mg maximum recommended dose for Amaryl. If the physician prescribed Amaryl in any of its available strengths and the pharmacist/nurse misinterpreted the drug as Ampyra, clarification of the physician's intent would be required as Amprya only available in 10 mg.

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale that minmizes the risk of the failure mode to occur**
Proprietary Name	**Strength**	**Usual Dose:**
Ampyra	**10 mg tablet**	**10 mg orally twice daily**
Agrylin (anagrelide hydrochloride) oral capsule 0.5 mg (1 mg capsule available only in generic formulation)	Orthographic similarity stems from sharing the same first letter (‘A’) and having the same number of down strokes in their name (‘g’ and ‘y’ in Agrylin vs ‘p’ and ‘y’ in Ampyra). Shared product characteristics include route of administration (oral) and potentially frequency of administration (twice daily)	Orthographic difference stems from the presence of the letter ‘m’ in Ampyra which separates the first letter from the first down stroke (‘p’) making this name look longer in handwriting samples. In contrast, there is no such separation between the first letter and the first down stroke in Agrylin and this name appears shorter. Additionally, Agrylin has an upstroke represented by ‘l’ and the proposed name, Ampyra lacks this characteristic. The recommended dose for Agrylin is 1 mg twice daily or 0.5 mg four times daily. Therefore, if a prescriber were to order ‘Ampyra 10 mg’ and the nurse/pharmacist misinterpreted the order as Agrylin 10 mg, this exceeds the maximum recommended single dose to be administered which is 2.5 mg. Conversely, if a prescriber were to order ‘Agrylin 1 mg’ and this were misinterpreted as Ampyra 1 mg, this dose is unachievable since the product is available only as 10 mg.
Amdry-C (chlorpheniramine maleate 8 mg, methscopolamine nitrate 2.5 mg, and 120 mg pseudoephedrine hydrochloride) extended release oral tablet	Orthographic similarity stems from same letters in first, second, fourth and fifth positions (A, M, R and Y) Both products could be prescribed as ‘1 tablet’ since they both exist in one strength. Overlapping product characteristics include route of administration (oral) and dosage form (tablet).	These names are orthographically different because of differences in the number and positions of their down-strokes. The name, Amdry-C, contains one down-stroke which appears near the end of the name whereas the proposed proprietary name ‘Ampyra’ has two sequential down-strokes in the middle of its name. Additionally, the modifier ‘C’ does not look like a lower case ‘a’ (in Amprya). The frequency of administration differs (once daily vs. twice daily)

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale that minmizes the risk of the failure mode to occur**
Proprietary Name	**Strength**	**Usual Dose:**
Ampyra	**10 mg tablet**	**10 mg orally twice daily**
Amdry-D (methscopolamine 2.5 mg and 120 mg pseudoephedrine) extended release oral tablet	Orthographic similarity stems from same letters in first, second, fourth and fifth positions (A, M, R and Y) Both products could be prescribed as '1 tablet' since they both exist in one strength. Overlapping product characteristics include route of administration (oral), dosage form (tablet), and frequency of administration (twice daily).	These names are orthographically different because of differences in the number and positions of their down-strokes. The name, Amdry-D, contains one down-stroke which appears near the end of the name whereas the proposed proprietary name 'Ampyra' has two sequential down-strokes in the middle of its name. Additionally, the modifier 'D' (in Amdry-D) does not look like a lower case 'a' (in Amprya). These differences will likely minimize confusion between this name pair.
Campral (acamprosate) delayed-release tablet 333 mg	Orthographic similarity stems from the similarity of the letters 'C' and 'A' in some handwriting samples. Overlapping product characteristics include dosage form (tablet) and route of administration (oral). Because both drug products exist in single strengths, the prescriber may refer to the dosage in number of tablets vs. identifying a specific strength.	Orthographic differences include the number and location of the down strokes and upstrokes in these names. The name Campral has one down-stroke ('p') in the middle of its name and an up-stroke ('l') at the end of its name. In contrast the proposed proprietary name, 'Ampyra', has no up-stroke but has two down-strokes ('py') in sequential order. These characteristics should help minimize confusion between these names. The frequencies of administration differ (twice daily vs. three times daily).

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale that minmizes the risk of the failure mode to occur**
Proprietary Name	**Strength**	**Usual Dose:**
Ampyra	**10 mg tablet**	**10 mg orally twice daily**
Compro (prochlorperazine) suppository 25 mg	Orthographic similarity stems from sharing the same combination of letters in similar positions Both drug products share the same frequency of administration (twice daily)	Orthographic difference stems from the existence of a second down stroke (represented by the letter 'y') in Ampyra which is not present in Compro. Confusion leading to medication errors is unlikely to occur because of the differences in dosage form (suppository vs. tablet) and route of administration (rectally vs. orally).
Inspra (eplerenone) oral tablet 25 mg, 50 mg	Orthographic similarity stems from the similarity of capital letters 'I' and 'A' in some handwriting samples as well as sharing the same last letter ('a'). Shared product characteristics include dosage form (tablet) and route of administration (oral).	Orthographic difference stems from the existence of a second down stroke (lower case 'y') in Ampyra and its role in making this name appear longer than the name Inspra. The strength must be specified for Inspra and neither one overlaps numerically with the strength for Ampyra. If 'Inspra 50 mg once daily' was prescribed and it was misinterpreted as 'Ampyra', the pharmacist/nurse would have to dispense/administer 5 tablets and the frequency of administration for Ampyra would be less than that recommended. The combination of these factors may prompt the pharmacist/nurse to clarify the prescriber's intent.
		(b) (4)

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Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale that minmizes the risk of the failure mode to occur**
Proprietary Name	**Strength**	**Usual Dose:**
Ampyra	**10 mg tablet**	**10 mg orally twice daily**
Onglyza (saxagliptin) oral tablet 2.5 mg, 5 mg	Orthographic similarity stems from the similarity of 'O' (Onglyza) and 'A' (Ampyra) in some handwriting samples and both names end in the letter 'a'. Shared product characteristics include dosage form (tablet) and route of administration (oral). Additionally, 10 mg is an achievable strength for Onglyza (2 x 5 mg tablets).	The name, Onglyza, contains an upstroke ('l') which is not present in Ampyra. Additionally, the first two down-strokes in Onglyza are separated by an upstroke (lower case 'l') vs the presence of two sequential down-strokes in the name Ampyra. These orthographic differences should help to minimize confusion between this name pair. Onglyza is taken once daily vs twice daily for Ampyra. Because Onglyza is available in two strengths, this information must be specified which will help to differentiate this drug product from Ampyra.
Apidra (insulin glulisine) Injection 100 units/mL	Orthographic similarity stems from sharing the same first letter ('A') and the same last two letters ('-ra') Both drug products have overlapping numerical strengths (10 mg vs. 100 units)	Orthographic differences include the existence of one upstroke in the name, 'Apidra' and the existence of two sequential down-strokes in the name, 'Ampyra'. These differences should help to distinguish these names. Differences in product characteristics such as dosage form (injection vs tablet), route of administration (intravenous or subcutaneous vs. oral), and frequency of administration (three times daily before a meal vs. twice daily) will minimize the risk of confusion leading to medication errors.
[redacted]		(b) (4)

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Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale that minmizes the risk of the failure mode to occur**
Proprietary Name	**Strength**	**Usual Dose:**
Ampyra	**10 mg tablet**	**10 mg orally twice daily**
Spiriva (tiotropium bromide) powder for inhalation 0.018 mg/ inhalation	Orthographic similarity stems from the similarity in the first letters (‘S’ and ‘A’) and the letters next to the last (‘v’ and ‘r’) in some handwriting samples. Both drug products are available as single dose and therefore may be prescribed as ‘one’ (tablet or inhalation) Drug products share route of administration (oral).	Orthographic difference stems from the presence of two down strokes in Ampyra (represented by ‘p’ and ‘y’) which are present in the middle of the name vs. one in Spiriva (‘p’) which is present in the prefix. Additionally, the ‘m’ and ‘y’ present in Ampyra makes this name look longer than Spiriva. Confusion leading to medication errors is unlikely to occur due to differences in product characteristics such as dosage form (powder vs. tablet), dose (18 mcg vs. 10 mg), route of administration (capsule for inhalation vs. oral ingestion) and frequency of administration (once daily vs. twice daily)
[redacted]	[redacted]	[redacted] (b) (4)

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale that minmizes the risk of the failure mode to occur**
Proprietary Name	**Strength**	**Usual Dose:**
Ampyra	**10 mg tablet**	**10 mg orally twice daily**
Cimzia (certolizumab pegol) injection 200 mg	Orthographic similarity stems from the similarity of the combination letters 'Ci-' (Cimzia) and 'A' (Ampyra) in some handwriting samples as well as sharing the letters 'm' and 'a' in similar locations within their names.	Orthographic differences stem from the differences in number of down-strokes. Cimzia has one ('z') and Ampyra has two which occur sequentially ('-py-'). Confusion leading to medication errors is unlikely to occur due to differences in product characteristics which include dosage form (injection vs. tablet), route of administration (subcutaneous vs. oral), strength (400 mg vs. 10 mg), and frequency of administration (weeks 2 and 4, then every 4 weeks vs. twice daily).
Acanya (benzoyl peroxide and clindamycin phosphate) topical gel 2.5%/1.2%	Orthographic similarity stems from having the same first and last letters ('A' and 'a').	Orthographic differences stem from the differences in number of down-strokes. Acanya has one ('y') and Ampyra has two down-strokes ('-py-') which occur sequentially. Confusion leading to medication errors is unlikely to occur due to differences in product characteristics which include dosage form (gel vs. tablet), route of administration (topical vs. oral), strength (2.5%/1.2% vs. 10 mg), and frequency of administration (once daily vs. twice daily). Additionally, instructions for use are likely to begin with 'Apply' vs. 'Take'.
[redacted]	[redacted]	[redacted] (b) (4)

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22250	ORIG-1	ACORDA THERAPEUTICS INC	FAMPRIDINE TABLETS

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

/s/

TODD D BRIDGES on behalf of DENISE V BAUGH
12/18/2009

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12/18/2009

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