CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22442Orig1s000

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Medication Error Prevention and Risk Management

Office of Surveillance and Epidemiology

Date:	May 24, 2011
Application Type/Number:	NDA 022442
Through:	Melina Griffis, R.Ph., Team Leader Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Anne C. Tobenkin, Pharm.D. Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name & Strength:	Rezira (Hydrocodone Bitartrate and Pseudoephedrine) Oral Solution, 5 mg/60 mg per 5 mL
Applicant/Sponsor:	Hawthorne Pharmaceuticals, Inc.
OSE RCM #:	2011-379

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

CONTENTS

1 INTRODUCTION

This re-assessment of the proposed proprietary name is written in response to the anticipated approval of this NDA within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Rezira, acceptable in OSE Reviews #2009-209, dated December 29, 2009 and #2009-2479, dated March 30, 2010.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the previous proprietary name review. We use the same search criteria previously used in the above stated reviews. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded two additional names (Prozac and Humira) thought to look similar to Rezira and represent a potential source of drug name confusion.

Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with the two names and lead to medication errors. This analysis determined that the name similarity between Rezira and Prozac and Humira was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN update. DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Rezira, as of May 13, 2011.

3 CONCLUSIONS AND RECOMMENDATIONS

The re-evaluation of the proposed proprietary name, Rezira, did not identify any vulnerabilities that would result in medication errors with the additional names noted in this review. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Rezira, 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, the Division of Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Nichelle Rashid, OSE Regulatory Project Manager, at 301-796-3904.

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4 REFERENCES

4.1 REVIEWS

1. OSE Review # 2009-209, dated December 29, 2009. Proprietary Name Review; Felicia Duffy, R.N, BSN, MSEd.
2. OSE Review # 2009-2479, dated March 30, 2010. Proprietary Name Review; Zachary Oleszczuk, PharmD.

4.2 DATABASES

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

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

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

   USAN Stems List contains all the recognized USAN stems.

5. *CDER Proposed Names List*

   Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis (DMEPA) for review. The list is updated weekly and maintained by DMEPA.

Appendix A: Risk of name confusion minimized by preventions listed.

Product name with potential for confusion	Similarity to proposed proprietary name	Strength and dosage form	Usual dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Rezira (Hydrocodone bitartrate and Pseudoephedrine)		**5 mg/60 mg per 5 mL oral solution**	**Adult (b) (4) (b) (4) (5 mL) q 4-5 hours prn, not to exceed 4 doses (20 mL) in 24 hours** (b) (4)	
Prozac (Fluoxetine hydrochloride)	Orthographic	10 mg, 20 mg, 40 mg capsule	10 mg to 80 mg by mouth once daily or 20 mg to 40 mg by mouth twice daily	*Orthographic differences* - Rezira has three letters after the downstroke vs. Prozac has two letters *Product characteristics* - Frequency of administration (every 4 to 6 hours vs. once daily) - Dose (5 mL (b) (4) vs. 1 capsule) - Strength (5 mg/60 mg per 5 mL vs. 10 mg, 20 mg, 40 mg) - Dosage form (solution vs. capsule)
Humira (Adalimumab)	Orthographic	20 mg, 40 mg prefilled syringes	20 mg or 40 mg subcutaneously every other week or 40 mg subcutaneously once a week	*Orthographic differences* - Beginning letter, 'R', in Rezira does not resemble beginning letter, 'H' in Humira *Product characteristics* - Frequency of administration (every 4 to 5 hours vs. once weekly or every other week) - Route of administration (oral vs. subcutaneous) - Strength (5 mg/60 mg per 5 mL vs. 20 mg, 40 mg) - Dosage form (solution vs. prefilled syringe, injection)

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/s/

MELINA N GRIFFIS
05/24/2011

CAROL A HOLQUIST
05/25/2011

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:	March 30, 2010
To:	Badrul Chowdhury, MD, Director Division of Pulmonary, Allergy, and Rheumatology Products
Through:	Denise Toyer, PharmD., Deputy Director Division of Medication Error Prevention and Analysis
From:	Zachary Oleszczuk, PharmD., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Rezira (Hydrocodone Bitartrate and Pseudoephedrine HCl) Oral Solution 5 mg/60 mg per 5 mL
Application Type/Number:	NDA 22442
Applicant:	Cypress Pharmaceuticals
OSE RCM #:	2009-2479

1 INTRODUCTION

This re-assessment of the proprietary name is written in response to the anticipated approval of NDA 22442 within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Rezira, acceptable in OSE Review #2009-209, dated December 29, 2009. The Division of Pulmonary, Allergy, and Rheumatology Products did not have any concerns with the proposed name, Rezira during the previous review of the proposed name and the Division of Drug Marketing, Advertising and Communication (DDMAC) found the name acceptable from a promotional perspective on February 12, 2009.

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 used the same search criteria outlined in OSE Review #2009-209, dated December 29, 2009, for the proposed proprietary name, Rezira. None of Rezira's product characteristics have been altered since our previous review thus, we did not re-evaluate previous names of concern. 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

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 25, 2010.

Additionally, the searches of the databases yielded one new name (Benicar), thought to look similar to Rezira and represent a potential source of drug name confusion. However, the findings of the FMEA indicate that the proposed name, Rezira, is not likely to result in name confusion with any of the identified names for the reasons presented in Appendix A.

4 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Rezira, is not vulnerable to name confusion that could lead to medication errors, nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Rezira, 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, the Division of Pulmonary, Allergy, and Rheumatology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

5 REFERENCES

1. Duffy, F. OSE Review #2009-209: Proprietary Name Review for Rezira. December 29, 2009.

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.

APPENDICES

Appendix A: Potential confusing name with numerical overlap in strength or dose with Rezira

Failure Mode: **Name confusion**	**Causes (could be multiple)**	**Effects**
Rezira **(Hydrocodone; Pseudoephedrine)** **Oral solution** **5 mg/60 mg per 5 mL**		**Usual dose:** **Adults** (b) (4) **5 mL orally every 4 to 6 hours as needed, not to exceed 4 doses (20 mL) in 24 hrs** (b) (4)
Benicar (olmesartan medoxomil) Dosage Form: Tablets Strength: 5 mg, 20 mg, and 40 mg Usual dose: 20 mg to 40 mg orally once daily	Orthographic similarity: (Both names contain the same number of upstrokes (one, 'B' vs. 'R'), the same number of dotted letters (one, 'i'), same second, fourth and 6th letter ('e', 'i', and 'a') and the 'B-' and 'R-' may appear similar if the B is not completely closed when scripted) Overlapping route of administration (oral) Numerical overlap in strength (5 mg vs. 5 mL)	Orthographic differences in the name in addition to the different frequencies of administration and units of measurement minimize the likelihood of medication error in the usual practice setting. *Rationale*: Although the beginning of each name may appear similar and both names share several overlapping letters, Benicar appears longer when scripted because the name 'Benicar' contains one additional letter (seven letters vs. six letters) than Rezira and the letter 'n' in Benicar elongates the name when scripted. Additionally, if the letter 'z' in Rezira is written with a downstroke, the downstroke will help differentiate the names from one another since Benicar does not contain a downstroke. Furthermore, although Benicar and Rezira share a route of administration (oral) and a similar numerical dose (5 mg vs. 5 mL), the frequencies of administration is different (once daily vs. every 4 to 6 hours as needed). The units of measurement (mg vs. mL or (b) (4) is also different. Rezira will likely be dosed by volume ((b) (4) 5 mL) whereas Benicar will be dosed in milligrams (i.e. 5 mg, 20 mg, or 40 mg). Since frequencies of administration and units of measurement typically appear on a written prescription these differences will help to minimize the risk of confusion between these two products.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22442	ORIG-1	CYPRESS PHARMACEUTICAL INC	REZIRA (b)(4) (HYDROCODONE BITARTRATE AND PSEU

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/s/

ZACHARY A OLESZCZUK
03/30/2010

DENISE P TOYER
03/31/2010

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 29, 2009
To:	Badrul Chowdhury, MD, Director Division of Pulmonary and Allergy Products
Through:	Kellie Taylor, PharmD, MPH, Associate Director Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Felicia Duffy, RN, BSN, MSEd, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name:	Rezira (Hydrocodone Bitartrate and Pseudoephedrine HCl) Oral Solution 5 mg/60 mg per 5 mL
Application Type/Number:	NDA 22442
Sponsor:	Cypress Pharmaceuticals
OSE RCM #:	2009-209

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CONTENTS

EXECUTIVE SUMMARY

Rezira is the proposed proprietary name for Hydrocodone Bitartrate and Pseudoephedrine HCl Oral Solution. 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. The Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective. Our evaluation identified concerns with another proposed proprietary from the same Applicant, (b) (4) (b) (4). However, the name (b) (4) has been determined to be unacceptable (see OSE review 2009-907) and therefore we consider Rezira acceptable.

This is considered a final review; however, if approval is delayed beyond 90 days from the date of this review, the proprietary name should be submitted for re-review.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a written request from Cypress Pharmaceuticals dated January 26, 2009, for an assessment of the proposed proprietary name, Rezira, regarding the promotional nature of the name and potential name confusion with other proprietary or established names in the usual practice settings.

1.2 REGULATORY HISTORY

On December 1, 2008, the Applicant formally submitted a request for proprietary name review for this application under the proposed proprietary name (b) (4). On January 6, 2009, the Division of Pulmonary and Allergy Products provided comments by facsimile to the Applicant:

(b) (4)

On January 26, 2009, the Applicant changed its proposed proprietary name request for this application to Rezira. The Applicant formally withdrew the proposed proprietary name, (b) (4), on January 29, 2009.

The Applicant also submitted the proposed proprietary name (b) (4) for a separate application (NDA 22-439) which contains hydrocodone, pseudoephedrine, and chlorpheniramine. In response to the above facsimile, the Applicant withdrew the proposed proprietary name, (b) (4) and changed its requested proposed proprietary name to (b) (4) is under separate review (OSE review #2009-907).

1.3 PRODUCT INFORMATION

Rezira is a combination product for oral administration that contains hydrocodone bitartrate and pseudoephedrine hydrochloride (5 mg/60 mg per 5 mL) formulated as an oral solution. The proposed indication is for (b) (4) relief of cough and (b) (4) relief of nasal congestion cough due to the common cold. The usual dose for (b) (4) adults is (b) (4) (5 mL) every 4 to 6 hours as needed, not to exceed 4 doses (20 mL) in 24 hours. (b) (4)

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(b) (4)

Rezira will be available in 480 mL bottles.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary names, Rezira. DMEPA also reviewed the proposed proprietary name, (b) (4) which is under separate review (OSE review #2009-907).

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'R' 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 Rezira, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (6 letters), upstrokes (one, capital letter 'R'), downstrokes (none, or one if the lower case 'z' is scripted with a downstroke), cross-strokes (none), and dotted letters (one, lower case 'i'). Additionally, several letters in Rezira 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 Rezira.

When searching to identify potential names that may sound similar to Rezira, the DMEPA staff search for names with similar number of syllables (three or four), stresses (RE-zi-ra or re-ZI-ra), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as '-zira' may sound like '-sira' (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's intended pronunciation of the proprietary name (\rezer-ə\) was taken into consideration, as this was provided with the proposed name submission. Although the intended pronunciation was provided, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

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

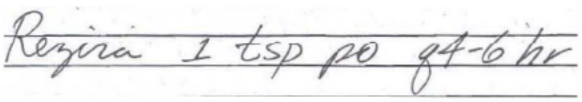
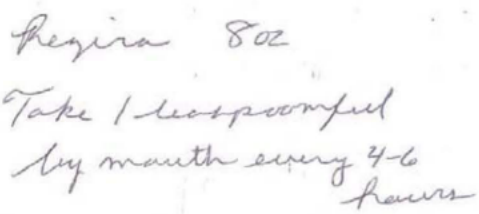
[1] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

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

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.

Figure 1. Rezira Rx Study (conducted on February 13, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order :  Outpatient Prescription: 	Rezira 8 ounce Take 1 teaspoonful by mouth every 4 to 6 hours

2.3 EXTERNAL DATABASE

For this product, the Applicant submitted a list of names from an external database, (b) (4), in search of similar names with the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided. When the external database identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 27 names as having some similarity to the name Rezira.

Twenty-three names were thought to look like Rezira, which include: Reopro, Prezista, Rezamid, (b) (4) Renova, Ranexa, Rescula, Rezulin, Rezyme, Rowasa, Pexeva, Rezipas, Remeron, Premarin, Nizoral, Boniva, Rogaine (b) (4) Revia, (b) (4) The remaining four names (b) (4), Rozerem, Balziva, and Rezine) were thought to look and sound similar to Rezira.

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DMEPA did not identify any United States Adopted Names (USAN) stems in the proposed name, Rezira, as of the last date searched on August 14, 2009.

3.2 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 Rezira.

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

DMEPA identified and evaluated a total of 23 practitioner respondents with none of the responses overlapping with an existing name. Eighteen participants interpreted the name correctly as "Rezira," with correct interpretation occurring in both the inpatient and outpatient written studies. The remainder of the written responses were misinterpretations of the proposed name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Rezira. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION

DMEPA notified the Division of Pulmonary and Allergy Products via e-mail that we had no objections to the proposed proprietary name, Rezira, on August 14, 2009. Per e-mail correspondence from the Division of Pulmonary and Allergy Products on August 25, 2009, they indicated that the review team concurs with our analysis.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

DMEPA reviewed the names supplied by the sponsor from the following databases: (b) (4) , Drug@FDA, NDC Directory, and Google. After reviewing the names from the databases, it was determined that there were no additional unique names identified that would necessitate additional evaluation. The Applicant submitted a listing of names from the (b) (4); however, no analysis or evaluation of the names listed was provided with the submission.

Independent searches by the primary Safety Evaluator identified one additional name, (b) (4) which was thought to look and sound similar to Rezira and represent a potential source of drug name confusion. Thus a total of 28 names were evaluated.

4 DISCUSSION

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective.

4.2 SAFETY ASSESSMENT

In evaluating Rezira's potential to look and sound similar to currently marketed products and products in the pipeline, we identified a total of 28 names as having some similarity to Rezira.

Four names were found to lack orthographic and/or phonetic similarity to the proposed name, Rezira, and were not evaluated further (see Appendix D).

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

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 24 names and lead to medication errors. This analysis determined that the name similarity between Rezira was unlikely to result in medication errors with the 23 products for the reasons presented in Appendices E through L. However, we find that the proposed name (b) (4) may cause confusion with Rezira (see Appendix M comparison of Rezira and (b) (4) (b) (4). However, this name, (b) (4) has been determined to be unacceptable and therefore, we consider Rezira acceptable (see OSE review 2009-907 for a detailed review of (b) (4).

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed proprietary name, Rezira, is not vulnerable to name confusion that could lead to medication errors, and it is not promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Rezira, 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, the Division of Pulmonary and Allergy Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

If you have further questions or need clarifications, please contact Carolyn Volpe, OSE Project Manager, at 301-796-5204.

5.1 COMMENTS TO THE APPLICANT

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

If **any** of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

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

6 REFERENCES

Database and Information Sources

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.

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

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

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

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

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 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 Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice.

[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.

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/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of 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.[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

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

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:

> ***"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 Sponsor 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 Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

The threshold set for objection to the proposed proprietary name may seem low to the Sponsor. 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 Sponsor can identify and rectify prior to approval to avoid patient harm.

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Rezira	Scripted may appear as	Spoken may be interpreted as
Capital 'R'	D, K, N, P	
lower case 'e'	i, o, r	any vowel
lower case 'z'	g, j, p, r, t, v, y	's'
lower case 'i'	e or r	any vowel
lower case 'r'	e, n, v	
lower case 'a'	e, i, n, o	any vowel

Appendix C: FDA Prescription Study Responses

Written Outpatient	**Written Inpatient**	**Verbal Prescription**
Rezira	Pregira	Rezera
Rezira	Pregra	
Rezira	Regira	
Rezira	Regina	
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		
Rezira		

Appendix D: Names lacking convincing look-alike and/or sound alike similarities with Rezira

Proprietary Name	Similarity to Rezira
Rezamid	Look
Reopro	Look
Premarin	Look
(b) (4)	Look

Appendix E: Discontinued or withdrawn product, no generics available

Proprietary Name	Similarity to Rezira	Source
Rezulin (Troglitazone)	Look	Drugs@FDA
Rescula (Unoprostone isopropyl)	Look	Drugs@FDA
Rezipas (Aminosalicylic acid resin complex)	Look	Drugs@FDA, Federal Register

Appendix F: Name of a dietary supplement

Proprietary Name	Similarity to Rezira	Source
Rezyme (vegetarian enzuyme)	Look	Natural Medicines Database

Appendix G: Proposed proprietary name of withdrawn NDA

Proprietary Name	Similarity to Rezira
(b) (4)	Look/Sound

Appendix H: Proprietary name of discontinued branded generic, established name is primarily used in standard practice

Proprietary Name	Similarity to Rezira	Source
Rezine (Hydroxyzine HCl)	Look/Sound	Micromedex

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

Product name with potential for confusion	Similarity to proposed proprietary name	Strength	Usual Dose (if applicable)
Rezira **(Hydrocodone; Pseudoephedrine) Oral solution**		**5 mg/60 mg per 5 mL**	**Usual dose:** **Adults** (b) (4) (b) (4) **(5 mL) q4-6 hrs prn, not to exceed 4 doses (20 mL) in 24 hrs** (b) (4)
Ranexa (Ranolazine) Extended-release tablets	Look	500 mg and 1000 mg	500 mg to 1000 mg po twice a day.
Prezista (Darunavir) Tablets	Look	75 mg, 300 mg, 400 mg, 600 mg	Adults: 600 mg to 800 mg po once daily. Children: 375 mg to 600 mg po twice a day.

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

Product name with potential for confusion	Similarity to proposed proprietary name	Strength	Usual Dose (if applicable)
Rezira **(Hydrocodone; Pseudoephedrine)** **Oral solution**		**5 mg/60 mg per 5 mL**	**Usual dose:** **Adults** (b) (4) (b) (4) **(5 mL) q4-6 hrs prn, not to exceed 4 doses (20 mL) in 24 hrs** (b) (4) (b) (4)
Pexeva (Paroxetine mesylate) Tablets	Look	10 mg, 20 mg, 30 mg, 40 mg	10 mg to 60 mg po once daily.
Remeron (Mirtazapine) Tablets Orally disintegrating tablet	Look	15 mg, 30 mg, 45 mg	15 mg to 45 mg po per day.
Revia (Naltrexone HCl) Tablets	Look	50 mg	50 mg po once daily.
Rozerem (Ramelteon) Tablets	Look/Sound	8 mg	8 mg po within 30 minutes of going to bed.

Product name with potential for confusion	Similarity to proposed proprietary name	Strength	Usual Dose (if applicable)
Rezira **(Hydrocodone; Pseudoephedrine) Oral solution**		**5 mg/60 mg per 5 mL**	**Usual dose:** **Adults** (b) (4) (b) (4) **(5 mL) q4-6 hrs prn, not to exceed 4 doses (20 mL) in 24 hrs** (b) (4)
Balziva (Ethinyl estradiol/ Norethindrone)	Look/Sound	0.035 mg/0.4 mg	Take 1 tablet po once daily.

Appendix J: Products with no overlap in strength, dose, dosage form and route of administration with Rezira

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength Dosage Form Route of Administration	Usual Dose (if applicable)
Rezira **(Hydrocodone and Pseudoephedrine)**		**5 mg/60 mg per 5 mL** **Oral solution** **Oral**	**Adults** (b) (4) **5 mL q4-6 hrs prn, not to exceed 4 doses (20 mL) in 24 hrs** (b) (4)
Renova (Tretinoin)	Look	0.02% and 0.05% Cream Topical	Apply to face once a day in the evening
Rowasa (Mesalamine)	Look	4 g per 60 mL Enema Rectal	Instill rectal enema once a day, and retain for approximately 8 hrs.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength Dosage Form Route of Administration	Usual Dose (if applicable)
Rezira **(Hydrocodone and Pseudoephedrine)**		**5 mg/60 mg per 5 mL** **Oral solution** **Oral**	**Adult** (b) (4) **5 mL q4-6 hrs prn, not to exceed 4 doses (20 mL) in 24 hrs** (b) (4)
Nizoral (Ketoconazole)	Look	1%, 2% Shampoo Topical	Apply shampoo, generously later, rinse thoroughly. Repeat every 3-4 days for up to 8 weeks.
Rogaine (Minoxidil)	Look	2%, 5% Solution, Foam Top.	Apply to scalp twice daily.
(b) (4)			

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

Appendix K: Products that overlap in (single) strength and dose with multiple differentiating product characteristics with Rezira

Product name with potential for confusion	Similarity to Rezira	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (vs. Product)
Rezira **Hydrocodone and pseudoephedrine**		**5 mg/60 mg per 5 mL**	(b) (4) **Adults** (b) (4) **po Q4-6 hr prn**	**Rezira (Hydrocodone/pseudoephedrine)**
(b) (4)				

Appendix L: Potential confusing name with numerical overlap in strength or dose with Rezira

Failure Mode: **Name confusion**	**Causes (could be multiple)**	**Effects**
Rezira **(Hydrocodone; Pseudoephedrine)** **Oral solution** **5 mg/4 mg/10 mg per** **5 mL**		**Usual dose:** **Adults** (b) (4) (b) (4) **(5 mL) q4-6 hrs prn, not to exceed 4 doses (20 mL) in 24 hrs** (b) (4)
Boniva (Ibandronate sodium) 2.5 mg, 150 mg tablets 1 mg/mL injection	Orthographic similarity: ('B-' and 'R-' may appear similar if the B is not completely closed when scripted; the endings '-iva' and '-ira' may appear similar when scripted; both contain 6 letters) Overlapping route of administration (oral) Numerical overlap in dose (2.5 mg vs. 2.5 mL)	Product differences minimize the likelihood of medication error in the usual practice setting. *Rationale*: Boniva is indicated for the prevention and treatment of osteoporosis in postmenopausal women. Although Boniva and Rezira may share a similar numerical dose of 2.5 mg vs. 2.5 mL, Boniva 2.5 mg is administered once daily, whereas Rezira will be administered every 4-6 hrs as needed. Additionally, Rezira will be dosed by volume (e.g., ½ tsp or 2.5 mL) whereas Boniva will be dosed in milligrams. Although Rezira and Boniva share a numerical overlap in dose (2.5 mg vs. 2.5 mL), the directions for use will help to differentiate and minimize the risk of confusion between Boniva and Rezira.

Appendix M

Comparison of Rezira (b) (4)

Proprietary Name	**Rezira**	(b) (4)
Established Name	Hydrocodone and **Pseudoephedrine**	(b) (4)
Sponsor	Cypress	
Indication	(b) (4) relief of cough and (b) (4) relief of nasal congestion due to the common cold	
Strength	Per 5 mL Hydrocodone **5 mg** Pseudoephedrine 60 mg	
How Supplied	480 mL	
Usual Dose and Frequency of Administration	Adults (b) (4) (5 mL) Q4-6 hrs as needed, not to exceed 4 doses (20 mL) in 24 hrs. (b) (4)	
Route of Administration	Oral	
Dosage Form	Oral solution	

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22442	ORIG-1	CYPRESS PHARMACEUTICAL INC	REZIRA (b)(4) (HYDROCODONE BITARTRATE AND PSEU

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

/s/

FELICIA DUFFY
12/29/2009

DENISE P TOYER on behalf of KELLIE A TAYLOR
12/29/2009

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12/29/2009

DENISE P TOYER on behalf of CAROL A HOLQUIST
12/29/2009