# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

**022439Orig1s000**

# PROPRIETARY NAME REVIEW(S)

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

# Proprietary Name Review--Final

| | |
|---|---|
| Date: | May 25, 2011 |
| Reviewer(s): | Richard Abate, RPh, MS, Safety Evaluator<br>Division of Medication Error Prevention and Analysis |
| Team Leader | Melina Griffis, RPh, Team Leader<br>Division of Medication Error Prevention and Analysis |
| Division Director | Carol Holquist, RPh<br>Division of Medication Error Prevention and Analysis |
| Drug Name and strength: | Zutripro (Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl) Oral Solution, 5 mg/4 mg/60 mg per 5 mL |
| Application Type/Number: | NDA 022439 |
| Applicant/sponsor: | Cypress Pharmaceuticals |
| OSE RCM #: | 2011-425 |

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# CONTENTS

## 1 INTRODUCTION

This re-assessment of the proposed proprietary name, Zutripro is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Zutripro, acceptable in OSE Review 2010-2734 dated February 23, 2011. DDMAC re-reviewed the proposed name on March 17, 2011 and had no concerns regarding the proposed name from a promotional perspective.

## 2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review # 2010-2734. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded one new name ((b) (4)***), thought to look or sound similar to Zutripro and represent a potential source of drug name confusion.

Failure Mode and Effects Analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with Zutripro and lead to medication errors. This analysis determined that the name similarity between Zutripro and the identified name was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of May 16, 2011.

## 3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Zutripro, did not identify any vulnerabilities that would result in medication errors with the additional name noted in this review. Thus, DMEPA has no objection to the proprietary name, Zutripro, 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.

If the Division has further questions or need clarifications, please contact Nichelle Rashid, OSE project manager, at 301-796-3904.

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## 4 REFERENCES


1. **OSE Review 2010-2734; Zutripro Proprietary Name Review, February 23, 2011, Abate, R.**

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/resources/doc/usan/stem-list-cumulative.pdf )***

   USAN Stems List contains all the recognized USAN stems.

4. ***Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request***

   Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

**Appendix A:** Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

| **Proposed name:**<br>**Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | **Strength:**<br>**5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **Usual dose:**<br>**For use adults 18 years and older:**<br>(b) (4) **(5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** |
|---|---|---|
| **Failure Mode: Name confusion** | **Causes (could be multiple)** | **Prevention of failure mode leading to medication error** |
| (b) (4) | | |

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/s/

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05/25/2011

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

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|---|---|
| Date: | February 23, 2011 |
| Application Type/Number: | NDA 022439 |
| Through: | Melina Griffis RPh, Team Leader<br>Carol Holquist, RPh, Director<br>Division of Medication Error Prevention and Analysis (DMEPA) |
| From: | Richard Abate, RPh, MS, Safety Evaluator<br>Division of Medication Error Prevention and Analysis (DMEPA) |
| Subject: | Proprietary Name Review |
| Drug Name(s): | Zutripro (Hydrocodone Bitartrate, Chlorpeniramine Maleate and Pseudoephedrine HCl) Oral Solution,<br>5 mg/4 mg/60 mg per 5 mL |
| Applicant: | Cypress Pharmaceuticals |
| OSE RCM #: | 2010-2734 |

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## CONTENTS

## EXECUTIVE SUMMARY

This review summarizes the Division of Medication Error Prevention and Analysis' evaluation of the proposed proprietary name, Zutripro (Hydrocodone Bitartrate, Chlorpeniramine Maleate and Pseudoephedrine HCl) Oral Solution. Our evaluation identified no concerns from a safety and promotional perspective that would render the name unacceptable. Thus, DMEPA finds the proposed proprietary name, Zutripro, acceptable for this product.

The proposed proprietary name, Zutripro, will be re-reviewed 90 days before approval of the NDA. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

## 1 BACKGROUND

### 1.1 INTRODUCTION

This review responds to a request from Cypress Pharmaceuticals on December 10, 2010, for an assessment of the proposed proprietary name, Zutripro, for NDA 022439 regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

### 1.2 REGULATORY HISTORY

Zutripro is a pending NDA with a PDUFA goal date of June 8, 2011. The Applicant previously submitted the several proposed names for this NDA which were either objected to by DMEPA or withdrawn by the Applicant as outlined in the table below.

| Proposed proprietary name | Outcome | Date of outcome | OSE review # |
|---|---|---|---|
| (b) (4) | Withdrawn by Applicant | January 29, 2009 | N/A |
| | DMEPA objected | January 11, 2010 | 2009-907 |
| | Withdrawn by Applicant | April 28, 2010 | N/A |
| | Withdrawn by Applicant | April 28, 2010 | N/A |
| | DMEPA objected | July 27, 2010 | 2010-930 |

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The Agency issued a Complete Response for the NDA June 11, 2010. Subsequently, the Applicant responded to the Complete Response December 8, 2010 for this current review cycle.

[redacted] These are summarized in the table below.

| NDA | Proposed proprietary name | DMEPA's opinion of proprietary name | Active ingredients | Status of NDA as of February 2011 |
|---|---|---|---|---|
| [redacted] | | | | |
| 22442 | Rezira*** | Acceptable | Hydrocodone Bitartrate and Pseudoephedrine HCl | Pending |

### 1.3 PRODUCT INFORMATION

Zutripro is an oral solution containing Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl (5 mg/4 mg/60 mg per 5 mL). It is indicated for the relief of cough and nasal congestion associated with the common cold and the relief of symptoms associated with upper respiratory allergies in adults 18 years and older. The dose of Zutripro is 5 mL [redacted] by mouth every four to six hours, not to exceed 20 mL in 24 hours. Zutripro is packaged in bottles containing 480 mL which are stored at room temperature (20° to 25° C.)

## 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

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information associated with the methodology for the proposed proprietary name, Zutripro.

### 2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'Z' 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 Zutripro, 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 (eight letters), upstrokes (two, capital letter Z and lower case t, down strokes (one, lower case p), cross strokes (one), and dotted (one). Additionally, several letters in Zutripro 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 Zutripro.

When searching to identify potential names that may sound similar to Zutripro, the DMEPA staff search for names with similar number of syllables (three), stresses (ZOO-treh-proh, zoo-TREH-proh or zoo-treh-PROH), and placement of vowel and consonant sounds. (See Appendix B) The Sponsor's intended pronunciation (zoo-truh-proh) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

### 2.2 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. (See Appendix C for samples and results)

## 3 RESULTS

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

### 3.1 DATA BASE AND INFORMATION SOURCES

The searches yielded a total of 26 names as having some similarity to the name Zutripro.

Twenty-one of the names were thought to look like Zutripro. These include: (b) (4) Astepro, Atripla, Avapro, Catapres, (b) (4) Cortizone (Cortizone 10), Cystagon,

[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)

Lexapro, Lipitor, Lofibra, Zaditor, Zaleplon, Zelapar, Zentrip, (b) (4)***, Zolinza, Zyloprim, Zyprexa, Zytiga***, and Zytopic. One of the names, Sumatriptan, was thought to sound like Zutripro. The remaining four names were thought to look and sound similar to Zutripro: Lutropin (Alfa), Nutripro, Nutropin, and (b) (4)***.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of January 6, 2010.

### 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 Zutripro.

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 PRESCRIPTION ANALYSIS STUDIES

A total of 23 practitioners responded with none of the responses overlapping with an existing name. Eleven of the participants interpreted the name correctly as "Zutripro," with correct interpretation occurring in the inpatient and outpatient written studies. The remainder of the written responses misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Zutripro. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

### 3.4 COMMENTS FROM THE DIVISION OF PULMONARY, ALLERGY AND RHEUMATOLOGY PRODUCTS (DPARP)

#### *3.4.1 Initial Phase of Review*

In response to the OSE, January 19, 2010 e-mail, Division of Pulmonary, Allergy and Rheumatology Products (DPARP) had no comments or issues related the proposed name at the initial phase of the name review.

#### *3.4.2 Midpoint of Review*

DMEPA notified the Division of Pulmonary, Allergy and Rheumatology Products via e-mail that we had no concerns with the proposed proprietary name, Zutripro, on February 4, 2010. Per e-mail correspondence from the Division of Pulmonary, Allergy and Rheumatology Products on February 7, they stated no additional concerns with the proposed proprietary name, Zutripro.

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### 3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in the identification of four additional names which were thought to look or sound similar to Zutripro and represent a potential source of drug name confusion.

The names identified to have look-alike similarities are Nitropress, Valtropin, Trilafon, and Trilipix.

Thus, we evaluated a total of 30 names: four identified by the primary safety evaluator, and 26 identified in section 3.1 above.

## 4 DISCUSSION

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

### 4.1 PROMOTIONAL ASSESSMENT

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

### 4.2 SAFETY ASSESSMENT

DMEPA evaluated 30 names for their potential similarity to the proposed name, Zutripro. No other aspects of the name were considered to pose potential confusion with the name. Five of these names were found to not be confused with Zutripro or used in the usual practice settings as described in Appendix D and thus not reviewed further. These names include: (b) (4)***, (b) (4)***, Nutripro, (b) (4)***, and Zytopic***.

Failure modes and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the 25 remaining names and lead to medication errors. This analysis determined that the name similarity between Zutripro and all of the remaining identified names was unlikely to result in medication error for the reasons presented in Appendices E through F.

## 5 CONCLUSIONS

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

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The proposed proprietary name, Zutripro, will be re-reviewed 90 days prior to NDA approval. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change. The Applicant will be notified of our findings via letter.

If you have further questions or need clarifications, please contact Nichelle Rashid, project manager, at 301-796-3904.

### 5.1 COMMENTS TO THE APPLICANT

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

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

If any of the proposed product characteristics as stated in your December 10, 2010 submission are altered, the proprietary name should be resubmitted for review.

## 6 REFERENCES


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

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

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

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

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

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

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

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

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

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

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

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

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

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

### *8. U.S. Patent and Trademark Office (http://www.uspto.gov)*

USPTO provides information regarding patent and trademarks.

### *9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)*

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

### *10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)*

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

### *11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)*

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

### *12. 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/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)*

USAN Stems List contains all the recognized USAN stems.

### *14. Red Book Pharmacy's Fundamental Reference*

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

### *15. Lexi-Comp (www.lexi.com)*

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

### *16. Medical Abbreviations Book*

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

## APPENDICES

### Appendix A:

FDA's Proprietary Name Risk Assessment considers the 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

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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.

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.

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

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

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. . (See Section 4 for limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the 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.

**Appendix B:** Letters with possible orthographic or phonetic misinterpretation

| Letters in Name, Zutripro | Scripted may appear as | Spoken may be interpreted as |
|---|---|---|
| Capital 'Z' | 2, F, I, L, T, or Y | 'C,' 'S,' or 'X" |
| lower case 'z' | g, n, m, q, r, s, or v | 'c,' 's,' or 'x' |
| lower case 'u' | a, n, o, v, y, or "ie" | any vowel |
| lower case 't' in combination 'tr' | f, r, or x 'br' | 'd' |
| lower case 'r' | n, s, t, or v | 'w' |
| Lower case 'i' | c, e, or l | any vowel |
| lower case 'p' | g, j, l, q, 'yn,' or 'ys' | 'b' |
| lower case 'o' | a, c u, or v | any vowel |

**Appendix C: Prescription study samples and results**

**Figure 1. Zutripro Study (conducted on January 18, 2011)**

| HANDWRITTEN REQUISITION MEDICATION ORDER | VERBAL PRESCRIPTION |
|---|---|
| Medication Order : Zutripro 5ml pō q6h prn cough | Zutripro 5 milliliters by mouth every six hours as needed for cough. |
| Outpatient prescription: Zutripro 4 oz Take 5mL po q4-6h prn | |

**FDA Prescription Study Responses.**

44 People Received Study
23 People Responded

Study Name: Zutripro

| INPATIENT | STRENGTH | VOICE | STRENGTH | OUTPATIENT | STRENGTH |
|---|---|---|---|---|---|
| Zutriplo | 5 mL | Dutripro | 5ml | Yutripro | none |
| Zutripro | 5 mL | Nutrepro | 5ml | Zutripro | |
| Zutripro | 5ml | Nutripro | 5ml | Zutripro | 4oz |
| Zutripro | 5 ml | Sutreprol | 5 mL | Zutripro | 4 oz |
| Zutripro | 5 ml | futripo | 500 ml | yutripro | 4 ounces |
| Zutripro | 5 mL | utryptal | 5 | zutcipro | |
| Zutripro | 5 mL | vitruperal | 5 ml | | |
| Zutripro | 5ml | | | | |
| Zvtripo | 5 ml | | | | |
| zutripro | 5 mL | | | | |

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

| Proprietary Name | Active Ingredient | Similarity to | Failure preventions |
|---|---|---|---|
| (b) (4) | | | |
| Nutripro | | Look and Sound | Not a medication: Identified as a website to purchase vitamins and other oral supplements for general health and weight loss. Also identified as a newsletter from Nestle. |
| (b) (4) | | | |
| Zytopic | Triamcinolone | Look | A prescription skin care kit containing multiple topical products. This kit is no longer marketed with no generic equivalents available. |

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

**Appendix E:** Risk of name confusion minimized by preventions listed. (Potential contributing causes highlighted by *italics*)

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Astepro<br>(Azelastine) | Look | 0.15%<br>*(Single Strength)* | *One* spray per nostril twice daily or two sprays per nostril daily. | **Orthographic difference:** The names begin with different appearing letters (A vs. Z).<br>**Dosage Form and route of administration:** Nasal spray vs. oral solution.<br>Frequency of use: Once or twice daily vs. every four to six hours.<br>**Product size:** 30 mL vs. 16 ounces. |
| Atripla<br>(Efavirenz, Emtricitabine and Tenofovir Disoproxil Fumerate) | Look | 600 mg/200 mg /300 mg tablets<br>(Single Strength) | *One* tablet *by mouth* once daily. | **Orthographic difference:** The names begin with different appearing letters (A vs. Z). Atripla includes the letter 'l' Providing a third upstroke which follows the letter 'p.'<br>**Dosage form:** tablet vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Avapro<br>(Ibesartan) | Look | 75 mg, 150 mg, and 300 mg tablets | *One* tablet *by mouth* once daily. | **Orthographic difference:** The names begin with different appearing letters (A vs. Z). Zutripro appears longer with more letters (8 vs. 6) and includes the letter 't' providing a second upstroke.<br>**Strength:** Multiple (75 mg. 150 mg, 300 mg) vs. single with no numeric overlap.<br>**Dosage form:** tablet vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |
| Catapres<br>(Clonidine HCl) | Look | 0.1 mg, 0.2 mg, and 0.3 mg tablets<br>TTS 1 (0.1 mg/24 hour), TTS 2 (0.2 mg /24 hour), and TTS 3 (0.3 mg/24 hours) patch | *One* tablet *by mouth* once or twice daily.<br>Apply *one* patch once a week | **Orthographic difference:** The names begin with different appearing letters (C vs. Z) and end with different appearing letters (-es vs. o).<br>**Strengths:** Multiple (0.1 mg, 0.2 mg, 0.3 mg and TTS-1, TTS-2, and TTS) vs. single with no numeric overlap.<br>**Dosage form:** tablet and patch vs. oral solution.<br>**Frequency of use:** Tablet - once or twice daily or patch - once weekly vs. every four to six hours. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Cortizone 10<br>(Hydrocortisone) | Look | 1 % Cream, ointment, liquid, lotion, and gel<br>*Single Strength* | Apply small amount topically to affected area three or *four times* daily | **Orthographic difference:** The names begin with different appearing letters (C vs. Z). Cortizone 10 appears longer with more letters (9 vs. 8) and a modifier (10).<br>**Dosage forms and route of administration:** Cream, ointment, liquid, lotion, and gel applied topically vs. oral solution. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Cystagon<br>(Cysteamine Bitartrate)<br>an orphan drug | Look | *50 mg* and 150 mg capsules | For the treatment of nephropathic cystinosis<br>Adults and children > 50 kg 500 mg cysteamine free base *by mouth every 6 hours.*<br>•Children weighing 41.4—50 kg (91—110 pounds): 450 mg cysteamine free base *by mouth every 6 hours.*<br>•Children weighing 32.3—40.9 kg (71—90 pounds): 400 mg cysteamine free base *by mouth every 6 hours.*<br>•Children weighing 23.2—31.8 kg (51—70 pounds): 350 mg cysteamine free base *by mouth every 6 hours.*<br>•Children weighing 18.6—22.7 kg (41—50 pounds): 300 mg cysteamine free base *by mouth every 6 hours.*<br>•Children weighing 14—18 kg (31—40 pounds): 250 mg cysteamine free base *by mouth every 6 hours.*<br>•Children weighing 9.5—13.6 kg (21—30 pounds): 200 mg cysteamine free base *by mouth every 6 hours.*<br>•Infants weighing 5—9 kg (11—20 pounds): 150 mg (*one* capsule) cysteamine free base *by mouth every 6 hours.*<br>•Infants weighing < 4.5 kg (<= 10 pounds): 100 mg cysteamine free base *by mouth every 6 hours.* | **Orthographic difference:** The names begin with different appearing letters (C vs. Z).<br>**Dosage form:** Capsules vs. oral solution.<br>**Dose in adult population:** Dose of Cystagon in adults requires multiple capsules and both strengths of product vs. (b) (4) 5 mL of Zutripro.<br>Cystagon is an orphan drug thus few patients take this product. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be <u>omitted</u> during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Lipitor<br>(Atorvastatin Calcium) | Look | 10 mg, 20 mg, *40 mg*, and 80 mg | *One* tablet *by mouth* daily. | **Orthographic difference:** The letters 'p' and 't' appears in juxtaposed order between these names.<br>**Strength:** Multiple (10 mg. 20 mg, 40 mg and 80 mg) vs. single (the numeric overlap occurs in the second ingredient of Zutripro).<br>**Dosage form:** tablet vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |
| Lofibra<br>(Fenofibrate) | Look | 54 mg and 160 mg tablets<br>67 mg, 134 mg and 200 mg capsules | *One* tablet or capsule *by mouth* daily. | **Orthographic difference:** Lofibra includes a 'b' providing a third upstroke and lacks a down stroke.<br>**Strength and Dosage form:** multiple strengths (54 mg, 160 mg tablets and 67 mg, 134 mg and 200 mg capsules) vs. single strength with no numeric overlap.<br>**Frequency of use:** daily vs. every four to six hours. |
| Nitropress<br>(Nitroprusside) | Look | *50 mg*/2 ml vial<br>*(single strength)* | Infuse 0.25 mcg/kg/min intravenously as a continuous infusion. | **Orthographic difference:** Nitropress include more letters (10 vs. 8) all of which follow the letter 'p' and add length to the name.<br>**Dose:** 0.25 mcg/kg/min vs. (b) (4) 5 mL.<br>**Dosage form and route of administration:** Injection in a vial which is diluted in an infusion by prior to intravenous administration vs. oral solution. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Sumatriptan<br>(established name for Alsuma, Imitrex, and Sumavel) | Sound | 25 mg, *50 mg* and 100 mg tablets,<br>*5 mg* and 20 mg nasal spray<br>4 mg/0.5 mL and 6 mg / 0.5 mL injection in a vial or pen. | *One* tablet by mouth at onset of headache, may repeat dose, once, after two hours.<br>*One (5 mg* or 20 mg) or two sprays (10 mg) at onset of headache, may repeat dose, once, after two hours.<br>*One* injection (4-6 mg) subcutaneously at onset of headache, may repeat dose, once, after one hour. | **Phonetic difference:** Sumatriptan includes two syllable not in Zutripro ("-ma-" and "-tan").<br>**Dosage form:** tablets, nasal spray and injection vs. oral solution.<br>**Frequency of use:** one time with one repeat dose vs. every four to six hours. |
| Trilafon<br>(Perphenazine)<br>Discontinued product with generic equivalents available | Look | 2 mg, *4 mg*, 8 mg and 16 mg tablets | *One* tablet *by mouth* three times daily. | **Orthographic difference:** Trilafon includes the letter 'f' which provides a third upstroke in the name.<br>**Strength:** multiple (2 mg, 4 mg, 8 mg and 16 mg) vs. single (the numeric overlap in strength occurs in the second ingredient of Zutripro).<br>**Dosage form:** tablets vs. oral solution.<br>**Frequency of use:** three times daily vs. every four to six hours. |
| TriLipix<br>(Fenofibric Acid) | Look | 45 mg and 135 mg capsules | *One* capsule *by mouth* daily | **Orthographic difference:** Zutripro includes the letter 't' which provides a cross stroke.<br>**Strength:** Multiple (45 mg and 135 mg) vs. single with no numeric overlap.<br>**Dosage form:** Capsule vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Zaditor<br>(Ketotifen | Look | 0.025%<br>*(Single Strength)* | *One* drop into affected eye every eight to twelve hours. | **Orthographic difference:** Zaditor include letters providing three upstrokes but no down strokes.<br>**Dosage form and route of administration:** ophthalmic solution vs. oral solution.<br>**Frequency of use:** every eight to twelve hours vs. every four to six hours. |
| Zaleplon<br>(established name for Sonata) | Look | *5 mg* and 10 mg capsules | *One* capsule *by mouth* daily, at bedtime. | **Orthographic difference:** Zaleplon includes two "l's" providing the second and third upstrokes but no cross stroke.<br>**Dosage form:** capsule vs. oral solution.<br>**Frequency of use:** daily at bedtime vs. every four to six hours. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>(b) (4) **(5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Zentrip<br>(Meclizine HCl) | Look | 25 mg oral strips<br>*single strength* | *One* or two strips (25 mg to *50 mg*) *by mouth* daily | **Orthographic difference:** Zutripro ends with the '-ro" following the 'p' adding length to the name.<br>**Dosage form:** Oral dissolving strip vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |
| (b) (4) | | | | |

*** **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) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be <u>omitted</u> during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Zolinza<br>(Vorinostat) | Look | 100 mg Capsules<br>*(Single strength)* | Three or four capsules (300 mg to 400 mg) *by mouth* daily.<br>Dose may be reduced to 300 mg by mouth five days a week. | **Orthographic difference:** Zutripro includes a 't' providing a cross stroke and two letters '-ro' following the down stroke.<br>**Dose:** Three or four (300 mg or 400 mg) vs. 5 mL (b) (4).<br>**Dosage form:** Capsules vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |
| Zyloprim<br>(Allopurinol) | Look | 100 mg and 300 mg tablets | *One* tablet *by mouth* daily | **Orthographic difference:** Zyloprim includes a down stroke provided by the 'y'. Zutripro includes a cross stroke provided by the 't.'<br>**Strength:** 100 and 300 mg vs. single with no numeric overlap.<br>**Dosage form:** tablet vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |

| Product name with potential for confusion | Similarity to Proposed Proprietary Name | Strength | Usual Dose (if applicable) | Failure Mode of name confusion leading to a medication error is prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described. |
|---|---|---|---|---|
| **Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | | **5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be <u>omitted</u> during the procurement and prescription steps of the medication use process)** | **For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** | |
| Zyprexa<br>(olanzepine) | Look | 2.5 mg, *5 mg,* 7.5 mg 10mg, 15 mg and 20 mg tablet and 10 mg vial for injection;<br>Zydis - *5 mg,* 10mg, 15 mg and 20 mg orally disintegrating tablets<br>Relprevv - 210 mg, 300 mg, and 405 mg extended-release powder for injection | *One* tablet (or Zydis) *by mouth* once daily.<br>2.5 mg to 10 mg intramuscularly as a single injection.<br>Relprevv One half to *one* syringe (150 mg to 300 mg) intramuscularly every two weeks or one syringe (405 mg) intramuscularly every four weeks. | **Orthographic difference:** Zyprexa includes two letters providing down strokes near the beginning of the name and include no upstrokes.<br>**Dosage form:** tablets, orally disintegrating tablets, and powder for injection vs. oral solution.<br>**Frequency of use:** daily, single dose, or every two or four weeks vs. every four to six hours. |
| Zytiga *** <br>(Abiraterone Acetate) | Look | 250 mg tablet<br>*(single strength)* | Four tablets (1000 mg) *by mouth* daily. | **Orthographic difference:** Zytiga*** includes fewer letters (6 vs. 8), appears shorter when scripted and includes a 'y' providing an additional down stroke immediately after the Z.<br>**Dose:** four tablets vs. 5 mL (b) (4)<br>**Dosage form:** tablets vs. oral solution.<br>**Frequency of use:** daily vs. every four to six hours. |

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

**Appendix F:** Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

| **Proposed name:**<br>**Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | **Strength:**<br>**5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **Usual dose:**<br>**For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** |
|---|---|---|
| **Failure Mode: Name confusion** | **Causes (could be multiple)** | **Prevention of failure mode leading to medication error** |
| Lexapro<br>(Escitalopram)<br>5 mg, 10 mg, 20 mg tablets and 5 mg/5 mL oral solution<br>Usual dose: 10 mg (one tablet or two teaspoons) by mouth once daily. Dose ranges from 5 mg to 20 mg. | **Orthographic similarity:** The names contain a similar number of letters (7 vs. 8) and have a similar length, the names begin with similar appearing letters when scripted (L vs. Z), and the names end with the same letter grouping "-pro."<br>Both products are available as a single strength oral liquid with an overlapping achievable dose (5 mL (b) (4)). | Zutripro includes a letter 't' in the third position providing an upstroke not seen in Lexapro.<br>Lexapro is also available as both tablets and oral solution. The most common strength used is 10 mg tablets.<br>Zutripro is taken as needed every four to six hours. Lexapro is taken daily usually but no more frequent than twice daily.<br>Lexapro oral solution is available in 8 ounce bottles, compared to Zutripro which is available in 16 ounce bottles. |

| **Proposed name:**<br>**Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | **Strength:**<br>**5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be omitted during the procurement and prescription steps of the medication use process)** | **Usual dose:**<br>**For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** |
|---|---|---|
| **Failure Mode: Name confusion** | **Causes (could be multiple)** | **Prevention of failure mode leading to medication error** |
| Lutropin (Alfa)<br>(established name for Luveris)<br>75 unit powder for injection in a kit with diluent.<br>Usual dose: 75 units subcutaneously daily for up to 14 days. | **Orthographic similarity**: Both names contain eight letters, Begin with similar appear letters (L vs. Z), share the letter grouping "utr" and include the letter 'p' in the sixth position.<br>**Phonetic similarity:** Both names include three syllables; the beginning letter in each name share a placement on the tongue and sonorance (L vs. Z); and the second syllable begins with same combination of consonants ('tr').<br>Both product are available in a single strength presentation | The entire established name for Luveris is two words, Lutropin alfa. Therefore, when written out completely, "alfa" will add length. Phonetic difference stems from the third syllable in Lutropin which ends with a consonant in rather than a vowel.<br>Lutropin is used in conjunction with Follitropin alfa to aid in follicular stimulation and development. Therefore , it use is limited to reproductive specialists for women with a specific hormonal deficiency causing infertility. Furthermore, it is an injectable product administered by the patient subcutaneously on a daily basis.<br>Zutripro is an oral liquid administered every four to six hours as needed for cold and cough. |

| **Proposed name:**<br>**Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | **Strength:**<br>**5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be <u>omitted</u> during the procurement and prescription steps of the medication use process)** | **Usual dose:**<br>**For use adults 18 years and older:**<br>**[redacted] (b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** |
|---|---|---|
| **Failure Mode: Name confusion** | **Causes (could be multiple)** | **Prevention of failure mode leading to medication error** |
| Nutropin<br>(Somatropin)<br>5 mg and 10 mg vials<br>Nutropin AQ 10 mg/2 mL vials<br>Nutropin AQ Pen 10 mg and 20 mg<br>Nutropin AQ Nuspin 5 mg/2 mL, 10 mg/2 mL and 20 mg/2 mL<br>Usual dose:<br>(Adults) 0.006 mg/kg given subcutaneously daily.<br>(pediatrics) 0.3 mg/kg/week subcutaneously divided daily over six or seven days. | **Orthographic similarity:** Both names contain eight letters, have similar length, share the letter grouping "utr" and include the letter 'p' in the sixth position.<br>**Phonetic Similarity:** Both names include three syllables; the beginning letter in each name share a placement on the tongue and sonorance, and the second syllable begins with same combination of consonants ('tr').<br>Share a numeric overlap (5 mg) in the strength presentation. | Nutropin in available in multiple packaging configurations and dosage forms. The name may include modifiers to distinguish the packaging configuration or device which helps to provide orthographic differentiation.<br>The Phonetic differences stem from the fact the third syllable in Lutropin which ends with a consonant rather than a vowel.<br>Zutripro is a single strength multiple ingredient oral liquid in which the strength is likely to be omitted. Zutripro is dosed 5 mL [redacted] (b) (4) every four to six hours as needed.<br>Nutropin is an injectable product administered subcutaneously daily or six day per week. The dose is administered by a pen or a small volume much less than 5 mL is drawn up into a syringe and administered. |

| **Proposed name:**<br>**Zutripro**<br>**(Hydrocodone Bitartrate, Chlorpheniramine Maleate, and Pseudoephedrine HCl)** | **Strength:**<br>**5 mg/4 mg/60 mg per 5 mL**<br>**(single strength product, thus the strength may be <u>omitted</u> during the procurement and prescription steps of the medication use process)** | **Usual dose:**<br>**For use adults 18 years and older:**<br>**(b) (4) (5 mL) by mouth every four to six hours as needed, Maximum daily dose 20 mL (four doses) in 24 hours.** |
|---|---|---|
| **Failure Mode: Name confusion** | **Causes (could be multiple)** | **Prevention of failure mode leading to medication error** |
| Valtropin<br>(Somatropin)<br>5 mg vial<br>Usual dose: (adults)<br>0.33 mg/kg/week divided and given subcutaneously daily.<br>Usual dose (pediatric) 0.23 mg/kg/week to 0.37 mg/kg/week divided and given subcutaneously daily. | **Orthographic similarity:** Both names contain a similar number of letters (9 vs. 8) and a similar length, begin with a similar appearing letter group ("Va-" vs. "Zu") when scripted, share the letter pair "tr," and include the letter 'p' in similar position.<br>Both are available as single strength products which include 5 mg in the strength presentation. | Valtropin includes the letter 'l' providing an additional upstroke.<br>Zutripro is a single strength multiple ingredient oral liquid in which the strength is likely to be omitted. Zutripro is dosed 5 mL (b) (4) every four to six hours as needed.<br>Valtropin is an injectable product administered subcutaneously daily. The dose, a small volume much less than 5 mL is drawn up into a syringe and administered.<br>Valtropin, although approved, has not been marketed in the U.S. |
| Zelapar<br>(Selegiline)<br>1.25 mg oral disintegrating tablet<br>Usual dose: One or two tablets (1.25 mg or 2.5 mg) by mouth daily | **Orthographic similarity:** Both names begin with the same letter (Z), the names have a similar number of letters (7 vs. 8) and have a similar length, and have an upstroke in the third position (l vs. t) and name include the letter 'p' in a similar position.<br>Both product are single strength and taken orally. | Zutripro includes a letter 't' in the third position providing a cross stroke not seen in Zelapar. Zutripro includes an additional letter and appears longer when scripted<br>Zelapar is a tablet administered once a daily while Zutripro is a oral liquid administered every four to six hours. |

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/s/

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