

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

202880Orig1s000

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: July 2, 2013

Reviewer: Denise V. Baugh, PharmD, BCPS
Division of Medication Error Prevention and Analysis

Team Leader: Lubna Merchant, PharmD, M.S.
Division of Medication Error Prevention and Analysis

Drug Name and Strengths: Zohydro ER (Hydrocodone Bitartrate) Extended-release Capsules
10 mg, 20 mg, 30 mg, 40 mg, and 50 mg

Application Type/Number: NDA 202880

Applicant: Zogenix, Inc.

OSE RCM #: 2012-2124

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

CONTENTS

1	INTRODUCTION.....	3
2	METHODS AND DISCUSSION.....	3
3	CONCLUSIONS.....	3
4	REFERENCES.....	4

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Zohydro ER 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, *Zohydro ER*, acceptable in OSE Review 2012-1388 dated September 12, 2012.

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 2012-1388. We note that none of the proposed product characteristics were altered. However, we evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. The searches of the databases yielded no new names thought to look or sound similar to Zohydro ER and represent a potential source of drug name confusion.

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 June 26, 2013.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Zohydro ER, did not identify any vulnerability that would result in medication errors with any additional name. Thus, DMEPA has no objection to the proprietary name, Zohydro ER, 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 Analgesia, Anesthetics, and Addictive Products (DAAAP) 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, Mark Liberatore, OSE Project Manager, at 301-796-2221.

4 REFERENCES

1. OSE Reviews

Baugh, D. Zohydro ER (Hydrocodone Bitartrate) Extended-release Capsules Proprietary Name Review. OSE Review # 2012-1388 dated September 12, 2012.

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/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?>)

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.

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

/s/

DENISE V BAUGH
07/02/2013

LUBNA A MERCHANT
07/02/2013

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

Proprietary Name Review

Date: September 12, 2012

Reviewer(s): Denise V. Baugh, PharmD, BCPS
Division of Medication Error Prevention and Analysis

Team Leader: Lubna Merchant, PharmD, M.S.
Division of Medication Error Prevention and Analysis

Deputy Director: Kellie Taylor, PharmD, MPH
Division of Medication Error Prevention and Analysis

Division Director: Carol Holquist, R.Ph.
Division of Medication Error Prevention and Analysis

Drug Name(s) and Strengths: Zohydro ER (Hydrocodone Bitartrate) Extended-release
Capsules
10 mg, 20 mg, 30 mg, 40 mg, and 50 mg

Application Type/Number: NDA 202880

Applicant: Zogenix, Inc.

OSE RCM #: 2012-1388

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

CONTENTS

1	INTRODUCTION.....	1
1.1	Regulatory History.....	1
1.2	Product Information.....	1
2.2	Safety Assessment.....	2
3.	CONCLUSIONS.....	6
3.1	Comments to the Applicant.....	6
4	REFERENCES.....	7
	APPENDICES.....	10

1 INTRODUCTION

This review evaluates the proposed proprietary name, Zohydro ER, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

DMEPA reviewed the proposed proprietary name, “Zohydro” and found this name to be unacceptable because the name does not include a modifier that identifies the extended release properties of the product (OSE Review # 2011-2862 dated February 2, 2012).

On February 15, 2012, the Applicant contacted DMEPA by e-mail correspondence to state why a modifier is not necessary for their name. Their reasons included: 1) the Applicant (b) (4)

(b) (4) 2) the absence of a modifier is consistent with the marketed products Exalgo and Embeda (which do not have an extended release modifier and for which there are no immediate release dosage forms), as well as Opana and Nucynta (which have modifiers, and were marketed after the introduction of their respective immediate release forms). Additionally, the Applicant expressed concerns with physicians dropping the modifier and writing only “Zohydro” on a prescription, leading to confusion about what product to dispense. Furthermore, the Applicant stated that they would use a ‘logo lockup’ on all their packaging, containers, and on promotional material for Zohydro to address DMEPA’s concern with communicating the extended release properties of the product.

On May 1, 2012, we held a teleconference with the Applicant, per their request, to discuss our rationale for this decision. We stated the availability of immediate release hydrocodone-containing products in the marketplace whose strengths overlap with that of Zohydro and whose dosage forms can be opened, crushed, divided, or chewed as reasons to include a modifier. Additionally, we noted that decisions to recommend the addition of a modifier to a proprietary name are made on a case by case basis based upon our Failure Modes and Effects Analysis of the name and product. Furthermore, the “logo lock up” would not be visible to prescribers and therefore they may not be aware of the extended release properties of this drug product as a result. In the absence of an immediate release ‘Zohydro’ product, the omission of the modifier will not have any consequences.

As a result of this meeting, on June 14, 2012, the Applicant submitted a new proposed proprietary name, “Zohydro ER” for our review. No product characteristics have been modified since the previous review was completed.

1.2 PRODUCT INFORMATION

The following product information is provided in the June 14, 2012, proprietary name submission:

- Active Ingredient: Hydrocodone bitartrate

- Indication of Use: Management of moderate to severe pain in patients requiring continuous, around-the-clock opioid analgesic for an extended period of time
- Route of Administration: Oral
- Dosage Form: Capsules
- Strengths: 10 mg, 20 mg, 30 mg, 40 mg, and 50 mg
- Dose and Frequency: Patients will be dosed based on their pain level and opioid tolerance with a frequency of every 12 hours
- How Supplied: Bottles of 100
- Storage: room temperature
- Container and Closure Systems: HDPE Bottles

2. RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA concurred with the findings of OPDP's promotional assessment of the proposed name. The Division of Anesthetics, Analgesics and Addictive Products (DAAAP) did not respond to OPDP's assessment at the time of this review.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the overall safety evaluation of the name.

2.2.1 United States Adopted Names (USAN)

The July 17, 2012 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant stated that the root name "Zohydro" incorporates the prefix of their corporate name "Zogenix" and the prefix of Hydrocodone. As stated in our previous review, although this naming convention is not a concern in this name, use of the prefix 'Zo' may affect the acceptability of future proposed proprietary names and needs to be limited to a single product to avoid confusion within the product line.

The Applicant also stated in their submission that the modifier "ER" is intended to convey the extended release properties of the product. Our evaluation of the modifier "ER" is described in Section 2.2.6.

2.2.4 FDA Name Simulation Studies

Twenty-eight practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed

products. We note that two participants dropped the modifier in their responses. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, June 28, 2012, e-mail, the Division of Anesthetics, Analgesics, and Addictive Products (DAAAP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Zohydro ER. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Zohydro ER identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

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

Look Similar			
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
(b) (4)	FDA	Hydro 35	FDA
Zaleplon	FDA	Hydro 40	FDA
Lachydrin	FDA	Zoladex	FDA
Zolpidem	FDA	Zytopic	FDA
Latuda	Primary Reviewer		
Look and Sound Similar			
Zohydro ER	FDA	Zohydro	FDA
(b) (4)	FDA	Zutripro	FDA

Our analysis of the thirteen names included in our evaluation from Table 1 considered the information obtained in the previous sections along with their product characteristics. We

determined all thirteen names will not pose a risk for confusion as described in Appendix D through E.

2.2.7 FMEA of the Modifier ‘ER’

During our initial review of the previously proposed proprietary name “Zohydro”, we evaluated if this extended-release product required a modifier to convey the extended-release nature of the product. We also evaluated whether or not the lack of a modifier raises a potential safety concern, given the overlapping product characteristics of this product to the currently marketed immediate-release formulations containing Hydrocodone (e.g., Vicodin, Lortab). We determined the applicant needed a modifier based on the following:

First, we identified extended-release products approved without a modifier in the proprietary name and reviewed documented errors relating to wrong technique and wrong frequency of administration. Wrong technique errors involved patients or practitioners, chewing, splitting, opening, or crushing the extended-release oral dosage forms when these products were intended to be administered intact. Wrong frequency errors involved the administration of the extended-release dosage form at intervals more frequent than labeled, (e.g. taking a once daily drug twice a day). Wrong technique and wrong frequency errors occurred despite the presence of clear labeling directives to administer the products intact and at the given intervals. Additionally, based on the case narratives we were unable to determine a definitive root cause of the errors. These reports included extended-release products that had overlapping product strengths with immediate-release formulations.

We then considered whether the lack of a modifier may actually contribute to practitioners’ and patients’ knowledge deficit about the extended-release properties of the drug products. As it relates to this product, this consideration led us to evaluate whether the addition of a modifier to the Zohydro name might help to avoid some of the wrong technique and wrong frequency errors.

With respect to wrong technique errors, we reviewed the Institute for Safe Medication Practices’ (ISMP) list of “Oral Dosage Forms That Should Not Be Crushed” to identify if a modifier exists that could possibly convey that an extended-release dosage form should not be divided, cut, crushed, or chewed. We focused our review on those names with modifiers that are commonly used to denote extended-release (e.g. ER, SR, CR, XR, XL, LA), since the Institute of Medicine has charged FDA and Industry to standardize abbreviations to the greatest extent possible. Our review found that this list contains a nearly equal number of extended-release drug products in which the proprietary name contains a modifier (n = 82) to extended-release products with drug names without modifiers (n = 84). Based on this information, we conclude that there is no standard single modifier currently on the market today that is definitively linked to the requirement that an extended-release product should not be manipulated prior to administration. Although a clear pattern did not emerge from our review of this list with modifiers, our medication error post-marketing experience with drug products marketed without a modifier in the proprietary name leads us to believe that the failure to include a modifier that conveys the extended-release properties of the drug may predispose the product to wrong technique and wrong frequency errors. Therefore, in some

circumstances, a modifier in the proprietary name of an extended-release product may help reduce the risk of these types of error.

In this circumstance, Zohydro has direct overlapping strengths with the currently marketed immediate-release hydrocodone-containing tablets (10 mg). Since Zohydro is an extended-release capsule that should be swallowed intact and the currently marketed hydrocodone-containing immediate release tablets (e.g., Lortab, Vicodin) can be opened, crushed, divided, or chewed, we determined that including a modifier may signal to healthcare practitioners that Zohydro differs from the currently marketed immediate-release hydrocodone formulations on the market. The presence of the modifier may prompt health care providers to consult the full prescribing information to determine if the product can be opened, crushed, divided, or chewed prior to administration. Additionally, since immediate release hydrocodone-containing products can be initiated twice daily, and this overlaps with the frequency of administration of the proposed extended-release product, a modifier may be used to communicate that a product is an extended-release dosage form and cannot be interchanged with the immediate-release hydrocodone products.

We recognized there were limitations to this approach since there is post-marketing evidence that modifiers have been omitted or overlooked; however, given the increased risks associated with Zohydro, the addition of a modifier may add an incremental measure of safety. Therefore, DMEPA requested the Applicant add an appropriate modifier to the proposed name, Zohydro.

The Applicant has proposed the modifier “ER” for this product and referenced the Institute for Safe Medication Practice’s (ISMP’s) List of Products with Drug Name Suffixes. We acknowledge currently several marketed extended-release products which use this modifier (e.g., Nucynta ER, Opana ER, VoSpire ER, Razadyne ER and Ultram ER). The Applicant cited the marketed names Opana ER and Nucynta ER as having the labeled meaning for extended-release. For both of these names, the frequency of administration is twice daily, which is the same proposed frequency of administration for Zohydro ER. However, the ER modifier has not been exclusively used for products administered twice daily since there are examples of “ER” products that are administered at other frequencies (e.g., Razadyne ER and Ultram ER are administered once daily, Metadate ER is administered three times daily), Although this modifier cannot be consistently linked to a frequency of administration, the ER modifier has not been cited as a contributing factor to wrong frequency errors in postmarketing reports. Therefore, the use of the modifier ER is suitable to convey the extended-release properties of your product.

Finally, post-marketing surveillance of medication errors has identified wrong drug errors that involve products with the same active ingredient and overlapping product characteristics, but different release mechanisms. Ideally, we recommend avoiding overlaps in strength for drug products that have the same active ingredient, but different formulations. However, since a strength modification is not feasible at this point in product development, the nomenclature, labels and labeling of this product might help to

communicate the product's extended-release properties and minimize the risk for medication errors.

Given the combination of factors considered above, we conclude that the proposed modifier, "ER", is appropriate for this product.

2.2.8. Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Division of Anesthetics, Analgesics, and Addictive Products (DAAAP) via e-mail on August 6, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Division of Anesthetics, Analgesics, and Addictive Products on August 14, 2012, they stated no additional concerns with the proposed proprietary name, Zohydro ER.

3. CONCLUSIONS

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

If you have further questions or need clarifications, please contact Mark Liberatore, OSE project manager, at 301-796-2221.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Zohydro ER, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your June 14, 2012 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

4 REFERENCES

1. OSE Review

Baugh, D. OSE Review # 2011-2862, Proprietary Name Review for Zohydro. February 2, 2012.

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. This database also lists the orphan drugs.

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.

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

USPTO provides information regarding patent and trademarks.

8. ***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.

9. ***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.

10. ***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.

11. ***Access Medicine*** (www.accessmedicine.com)

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. ***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.

13. ***Red Book*** (www.thomsonhc.com/home/dispatch)

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

14. ***Lexi-Comp*** (www.lexi.com)

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

13. ***Medical Abbreviations*** (www.medilexicon.com)

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

17. ***CVS/Pharmacy*** (www.CVS.com)

This database contains commonly used over the counter products not usually identified in other databases.

17. Walgreens (www.walgreens.com)

This database contains commonly used over the counter products not usually identified in other databases.

18. Rx List (www.rxlist.com)

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! And Bing, and returns the most relevant results to the search.

20. Natural Standard (<http://www.naturalstandard.com>)

Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

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

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

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

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

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

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

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

² 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		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> 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/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

12. Γ Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

13. Γ FDA Prescription Simulation Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

14. **Comments from Other Review Disciplines**

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

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

15. **Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.³ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

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

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

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

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

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

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

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

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the

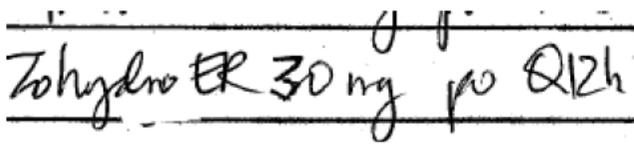
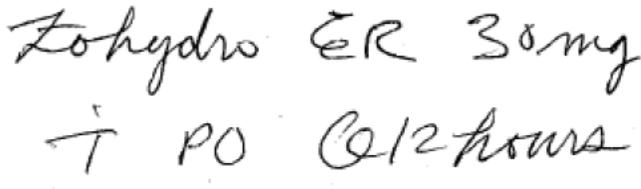
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Zohydro ER	Scripted May Appear As	Spoken May be Interpreted as
Z	2, C, f, I, L, M, T, S, V, Y, X	C, S, X
o	a, c, e, u	Combination letters “-oh-” or “-oe-”
h	k, b, n, L	Silent
y	f, p, u, v, x, Z	e, i, u, eye
d	cl	b, t
r	s, n, e, v	
o	a, c, e, u	Combination letters “-oh-” or “-oe-”
E	C, f	ee
R	B, Pr, K	WR

Appendix C: Prescription Simulation Samples and Results

Figure 1. Zohydro ER Study (Conducted on June 29, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>“Zohydro ER 30 mg Take 1 by mouth every 12 hours Dispense # 60”</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
FOHYDRO ER	0	0	3	3
XOHYRO ER	0	1	0	1
ZOHYDNO ER	1	0	0	1
ZOHYDRO	1	0	1	2
ZOHYDRO ER	6	6	8	20
ZOHYDRO-ER	0	1	0	1

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 Zohydro ER	Failure preventions
(b) (4)	Gabapentin Enacarbil	Orthographic similarity	(b) (4) was an alternate proprietary name for the proposed name (b) (4). DMEPA concurred with the Office of Prescription Drug Products (OPDP) which found (b) (4) unacceptable because the name (b) (4) the efficacy of the product (OSE Review # 2009-936 dated June 17, 2009). NDA 022399 was approved April 6, 2011 with the proprietary name, Horizant.
Zohydro ER	Not applicable	Orthographic and phonetic similarity	Name under evaluation in this review
(b) (4)	Not applicable	Orthographic and phonetic similarity	Alternate proposed proprietary name for Zohydro ER
Zohydro	Not applicable	Orthographic and phonetic similarity	DMEPA found the proposed proprietary name 'Zohydro' unacceptable because of the absence of a modifier to communicate its extended release properties (OSE Review # 2011-2862 dated February 2, 2012).

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

<p>Proposed name: Zohydro ER</p> <p>Dosage Form(s): Extended-release Capsule</p> <p>Strength(s): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual Dose: Dose is titrated based upon pain level and opioid tolerance; frequency is twice daily (every 12 hours)</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Zolpedim (Established name for Ambien)</p> <p>Tablet: 5 mg, 10 mg</p> <p>Extended Release tablet: 6.25 mg, 12.5 mg</p> <p>Sublingual Tablet: 1.75 mg, 3.5 mg, 5 mg, 10 mg</p> <p>Oral Metered Spray: 5 mg per spray</p> <p><u>Usual dose:</u></p> <p>10 mg immediately before bedtime (immediate release tablet, sublingual tablet, and oral spray); 1.75 mg for women and 3.5 mg for men once per night (sublingual)</p> <p>12.5 mg immediately before bedtime (extended release tablet)</p>	<p>Orthographic similarities stem from sharing the same first two letters (Zo) and the fact that both names have two up strokes ('l' and 'd' vs. 'h' and 'd') and a single down stroke ('p' vs. 'y').</p> <p>Overlapping product characteristics include strength (10 mg), and dosage form (tablet).</p>	<p>The two letters following the last up stroke in the marketed name, Zolpidem ('em') and in the proposed name, Zohydro ('ro') are not orthographically similar when written. Additionally, the presence of the modifier, 'ER' if written at the end of the name, Zohydro, gives this name a longer appearance vs. Zolpidem.</p>

<p>Proposed name: Zohydro ER</p> <p>Dosage Form(s): Extended-release Capsule</p> <p>Strength(s): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual Dose: Dose is titrated based upon pain level and opioid tolerance; frequency is twice daily (every 12 hours)</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Hydro 35 (Urea) topical Aerosol foam 35%</p> <p><u>Usual dose:</u> Apply to affected area (s) twice daily</p>	<p>Orthographic similarity stems from sharing the letters ‘Hydro’ in their names.</p> <p>Overlapping product characteristic includes the frequency of administration (twice daily).</p> <p>Both names have one route of administration and therefore this information need not be included on a medication order to dispense/administer either drug product.</p>	<p>The two letters (‘Zo’) which precedes the letter ‘h’ (in Hydro) gives the proposed name, Zohydro a longer appearance. Additionally, their modifiers (35 vs. ER) do not look similar when scripted.</p>
<p>Hydro 40 (Urea) topical Aerosol foam 40%</p> <p><u>Usual dose:</u> Apply to affected area (s) twice daily</p>	<p>Orthographic similarity stems from sharing the letters ‘Hydro’ in their names.</p> <p>Overlapping product characteristic includes the frequency of administration (twice daily).</p> <p>Numerical overlap in strength exists (40% vs. 40 mg).</p> <p>Both names have one route of administration and therefore this information need not be included on a medication order to dispense/administer either drug product.</p>	<p>The two letters (‘Zo’) which precedes the letter ‘h’ (in Hydro) gives the proposed name, Zohydro a longer appearance. Additionally, their modifiers (40 vs. ER) do not look similar when scripted</p>

<p>Proposed name: Zohydro ER</p> <p>Dosage Form(s): Extended-release Capsule</p> <p>Strength(s): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual Dose: Dose is titrated based upon pain level and opioid tolerance; frequency is twice daily (every 12 hours)</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Zytopic (Triamcinolone Acetonide) Cream 0.1%</p> <p>Zytopic is no longer available in the marketplace, but generic products exist which may be used as substitutes</p> <p><u>Usual dose:</u></p> <p>Apply to the affected area(s) 2 to 3 times per day</p>	<p>Orthographic similarity stems from sharing the same first letter (Z).</p> <p>One overlapping product characteristic is potentially the frequency of administration (twice daily).</p> <p>Both drug products have a single route of administration and therefore this information is not necessary on a medication order to dispense/administer either drug product.</p>	<p>The marketed drug, Zytopic includes two down strokes ('y' and 'p') in the second and fifth positions whereas the proposed name, Zohydro has two up strokes ('h' and 'd') in the third and fifth positions giving these names different shapes.</p>

<p>Proposed name: Zohydro ER</p> <p>Dosage Form(s): Extended-release Capsule</p> <p>Strength(s): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual Dose: Dose is titrated based upon pain level and opioid tolerance; frequency is twice daily (every 12 hours)</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Zaleplon Capsule (established name for the proprietary name, Sonata)</p> <p>5 mg, 10 mg</p> <p>Usual dose:</p> <p>10 mg immediately before bedtime</p>	<p>Orthographic similarity stems from the fact that both names begin with the same letter ('Z'), have two up strokes ('l' and 'l' vs. 'h' and 'd') and one down stroke ('p' vs. 'y') within their names.</p> <p>One overlapping product characteristic is the route of administration (oral).</p> <p>Additionally, numerical overlap in strengths exists (10 mg and 5 mg vs. 50 mg) and these names have achievable strengths (for example, two to five 10 mg tablets of Zaleplon may be used to achieve 20 mg to 50 mg of Zohydro).</p>	<p>The proposed proprietary name, Zohydro, includes sequential up strokes and down strokes ('hyd') in its infix whereas the up and down strokes in the marketed name, Zaleplon are interrupted by a lower case 'e' (e.g., Zaleplon). Additionally, the presence of the modifier, 'ER' if written at the end of the name, Zohydro, gives this name a longer appearance vs. Zolpidem.</p> <p>One differing product characteristics is the frequency of administration (before bedtime vs. twice daily).</p> <p>Preliminary drug usage data suggests that this drug name, Zaleplon, is not widely prescribed and therefore, there is little opportunity for confusion between the name, Zaleplon and Zohydro.</p>

<p>Proposed name: Zohydro ER</p> <p>Dosage Form(s): Extended-release Capsule</p> <p>Strength(s): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual Dose: Dose is titrated based upon pain level and opioid tolerance; frequency is twice daily (every 12 hours)</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Lac-Hydrin (Ammonium Lactate) Lotion or Cream 12%</p> <p><u>Usual dose:</u> Apply to the affected area(s) twice daily</p>	<p>Orthographic similarity stems from the similar appearance of their first letters ('L' vs. 'Z') in some handwriting styles and the fact that they share the same combination of letters (-hydr-) in similar positions within their names.</p> <p>One overlapping product characteristic is the frequency of administration (twice daily).</p>	<p>Differing product characteristics include the dose (non-specific vs. one capsule) and the route of administration (topical (to skin) vs. oral). Additionally, the adjectives used to describe administration of these drug products may differ (e.g., "Apply" to affected area(s) vs. "Give" one capsule).</p> <p>Zohydro is available in greater than one strength and this information would be necessary to dispense/administer the drug as intended</p>
<p>Zutripro (Chlorpheniramine and Hydrocodone and Pseudoephedrine) Oral Solution 4 mg/5 mg/60 mg per 5 mL</p> <p><u>Usual dose:</u> 5 mL every 4 hours to 6 hours as needed, not to exceed 20 mL in 24 hours</p>	<p>Orthographic similarity stems from sharing the same first letter ('Z') and the last two letters ('-ro').</p>	<p>The proposed proprietary name, Zohydro, contains two up strokes sandwiched between one down stroke ('hyd') whereas the marketed name, Zutripro has a single up stroke in the third position ('t') and a down stroke in the sixth position ('p') of its name. Additionally, the presence of the modifier, 'ER' if written at the end of the name, Zohydro, gives this name a longer appearance vs. Zolpidem.</p> <p>Differing product characteristics include the dose (one teaspoonful vs. one capsule) and the frequency of administration (every 4 hours to 6 hours vs. every 12 hours).</p> <p>Zohydro is available in several different strengths and therefore this information must be provided to dispense/administer the drug as intended.</p>

<p>Proposed name: Zohydro ER</p> <p>Dosage Form(s): Extended-release Capsule</p> <p>Strength(s): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual Dose: Dose is titrated based upon pain level and opioid tolerance; frequency is twice daily (every 12 hours)</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Zoladex (Goserelin Acetate) Implant</p> <p>3.6 mg, 10.8 mg</p> <p><u>Usual dose</u> :</p> <p>3.6 mg subcutaneously every 28 days or 10.8 mg subcutaneously every 12 weeks</p>	<p>Orthographic similarity stems from the fact that both names begin with the same first two letters ('Zo') and both names have two up strokes ('l' and 'd' vs. 'h' and 'd') in the same positions within their names.</p>	<p>The proposed name, Zohydro, includes a down stroke ('y') in the fourth position, which gives this name a different shape from the marketed name, Zoladex. Additionally, the last two letters of these names ('ex' vs. 'ro') do not look similar when written. Additionally, the presence of the modifier, 'ER' if written at the end of the name, Zohydro, gives this name a longer appearance vs. Zolpidem.</p> <p>Differing product characteristics include dose (3.6 mg and 10.8 mg vs. 10 mg, 20 mg, 30 mg, 40 mg, and 50 mg) and frequency of administration (every 28 days or every 12 weeks vs. twice daily).</p> <p>Zoladex and Zohydro are available in different strengths and this information must be clarified by the prescriber prior to dispensing/administering the medication.</p>

<p>Proposed name: Zohydro ER</p> <p>Dosage Form(s): Extended-release Capsule</p> <p>Strength(s): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual Dose: Dose is titrated based upon pain level and opioid tolerance; frequency is twice daily (every 12 hours)</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Latuda (Lurasidone Hydrochloride) Tablet</p> <p>20 mg, 40 mg, 80 mg</p> <p><u>Usual dose</u> :</p> <p>40 mg to 160 mg per day</p>	<p>Orthographic similarity stems from the similar appearance of their first letters ('L' vs. 'Z') in some handwriting styles and the fact that they both have two up strokes ('t' and 'd' vs. 'h' and 'd') in the same positions within their names.</p> <p>Overlapping product characteristics include the strength (20 mg and 40 mg), the route of administration (oral), and potentially the frequency of administration (twice daily).</p>	<p>The proposed name, Zohydro, includes a down stroke ('y') in the fourth position, which gives this name a different shape from the marketed name, Latuda. Additionally, the presence of the modifier, 'ER' if written at the end of the name, Zohydro, gives this name a longer appearance vs. Latuda.</p>

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

/s/

DENISE V BAUGH
09/12/2012

LUBNA A MERCHANT
09/12/2012

CAROL A HOLQUIST
09/12/2012