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RESEARCH**

APPLICATION NUMBER:

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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

Date: October 5, 2012

Reviewer: Loretta Holmes, BSN, PharmD
Division of Medication Error Prevention and Analysis

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Drug Name and Strength: Adasuve (Lorazepam) Inhalation Powder
10 mg

Application Type/Number: NDA 022549

Applicant: Alexza Pharmaceuticals, Inc.

OSE RCM #: 2012-1650

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Adasuve, 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

The proposed name, Adasuve, was previously reviewed in OSE Reviews 2010-371 and 2011-4069 and found acceptable. The application received a Complete Response (CR) on October 8, 2010 and the Applicant submitted a response to the CR on August 4, 2011. The application again received a CR on May 2, 2012 and the Applicant submitted a response to the CR on June 21, 2012. A request for proprietary name review was submitted on July 16, 2012.

1.2 PRODUCT INFORMATION

The following product information is provided in the July 16, 2012 submission. The product characteristics have changed since our previous review of the name. These changes include withdrawal of the 5 mg strength and dose, updated indication language, and a more restrictive frequency of administration.

- Active Ingredient: Loxapine
- Indication of Use: Acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults
- Route of administration: Oral Inhalation
- Dosage form: Inhalation Powder
- Strength: 10 mg
- Dose and Frequency of Administration: 10 mg by oral inhalation using an inhaler. Administer only a single dose within any 24-hour period.
- How Supplied: Single-use, disposable inhaler unit containing 10 mg of Loxapine, provided in a sealed foil pouch. Supplied in a carton containing 5 units.
- Storage: 15° to 30°C (59° to 86° F)
- Pronunciation: ADD-uh-soov

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 and the Division of Psychiatry Products (DPP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The September 21, 2012 search of the United States Adopted Name (USAN) stems did not identify a USAN stem present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

According to the Applicant, the proposed proprietary name has no derivation. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication errors.

2.2.3 FDA Name Simulation Studies

Eighty-four practitioners participated in DMEPA's prescription studies. Twelve participants in the verbal study misinterpreted the letter "d" as the letter "t". Eight participants in the inpatient or outpatient studies misinterpreted the letter "u" as the letter "i" and seven participants in these studies misinterpreted the letter "v" as the letter "r". See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, August 9, 2012 e-mail, the Division of Psychiatry Products (DPP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 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, Adasuve. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Adasuve, identified by the primary reviewer and the Expert Panel Discussion (EPD). Table 1 also includes the names identified by (b) (4) not identified by DMEPA, that require further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and External Name Study if applicable)

Look Similar					
Name	Source	Name	Source	Name	Source
Abreva	EPD Panel	Abraxane	EPD Panel	Advicor	EPD Panel
Adoxa	EPD Panel (b) (4)	Aclaro	EPD Panel	Adcirca	EPD Panel

Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
(b) (4)	EPD Panel	Aclovate	EPD Panel	(b) (4)	EPD Panel
(b) (4)	EPD Panel	Actical	EPD Panel	Actanol	EPD Panel
Actemra	EPD Panel	Ablavar	EPD Panel	Actonel	EPD Panel
Acticin	EPD Panel	Alsuma	EPD Panel	Absorica	EPD Panel
Activase	EPD Panel	Achara	EPD Panel	Adocaine	EPD Panel
Adagen	EPD Panel	Alavert	EPD Panel (b) (4)	Abacavir	EPD Panel
Ultrase	EPD Panel	Alinia	EPD Panel	(b) (4)	EPD Panel
Aleve	EPD Panel	Adagin	EPD Panel	Aluvea	EPD Panel
Ativan	EPD Panel	Adalat	EPD Panel (b) (4)	Udamin	EPD Panel
Antara	EPD Panel	Adefovir	EPD Panel (b) (4)	Alcaine	EPD Panel
Atacand	EPD Panel	Antabuse	EPD Panel	AdreView	EPD Panel
Adacel	EPD Panel (b) (4)	Sitavig***	EPD Panel	Acanya	EPD Panel
Albenza	EPD Panel	Ciclesonide	EPD Panel	Stalevo	EPD Panel
Cida-Stat	EPD Panel	Adapin	EPD Panel	Amidate	EPD Panel
Aclamen	EPD Panel	Adcentris	EPD Panel	Cidofovir	EPD Panel
Stavzor	EPD Panel	Azasan	EPD Panel	Advera	EPD Panel
Alvesco	EPD Panel	Aldara	EPD Panel	Pediasure	(b) (4)
Advair	(b) (4)	Adderall	(b) (4)	Atarax	(b) (4)
Aldomet	(b) (4)	Altabax	(b) (4)	Alteplase	(b) (4)

Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Advil	(b) (4)	Atorvastatin	(b) (4)	Atropine	(b) (4)
Avastin	(b) (4)	Adenosine	(b) (4)		

Our analysis of the 68 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics. We determined these 68 names will not pose a risk for confusion as described in Appendices D and E.

2.2.6 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Psychiatry Products via e-mail on September 17, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Psychiatry Products on September 23, 2012, they stated no additional concerns with the proposed proprietary name, Adasuve.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Sandra Griffith, OSE Project Manager, at 301-796-2445

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Adasuve, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your July 16, 2012 submission are altered, the proposed name must be resubmitted for review. Additionally, the proposed proprietary name must be re-reviewed 90 days prior to the approval of the application. The conclusions upon re-review are subject to change.

4 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. 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.

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. ***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 Pharmacy's Fundamental Reference**

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.

15. **Medical Abbreviations Book**

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

16. **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.

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.).

2. 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 Division of Drug Marketing, Advertising, and Communications (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.

3. 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.

4. 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.

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, 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

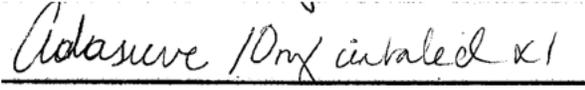
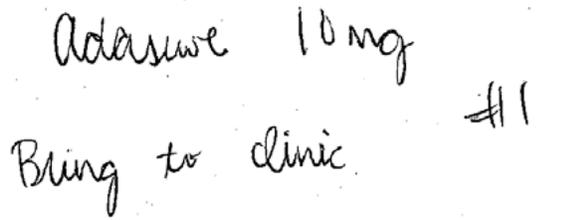
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval 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 NAME	Scripted May Appear as	Spoken May Be Interpreted as
Capital Letter 'A'	'O', 'S', 'D', 'C', 'T'	Any vowel
Lower case 'a'	'E', 'c', 'd', 'o', 'u', 'n'	Any vowel
Lower case 'd'	'el', 'cl', 'f', 't'	't'
Lower case 'a'	'E', 'c', 'd', 'o', 'u', 'n'	Any vowel
Lower case 's'	'v', 'r', 'c', 'g'	'x', 'z'
Lower case 'u'	'a', 'n', 'v'	Any vowel
Lower case 'v'	'r', 'u', 'n', 'w', 'k', 'z'	'w', 'z', 'b', 'th'
Lower case 'e'	'a', 'c', 'i', 'l', 'o'	Any vowel
"Ad"		'Add', 'Att'
"sue"		'suv', 'soof', 'soove'

Appendix C: Prescription Simulation Samples and Results

Figure 1. Adasuve Study (Conducted on August 6, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Inpatient Medication Order:</u></p> 	<p>Adasuve 10 mg Bring to clinic Dispense # 1</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

				175 People Received Study
				84 People Responded
Study Name: Adasuve				
Total	24	27	33	
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
?	0	1	1	2
ADASERVE	0	0	1	1
ADASEURE	0	0	1	1
ADASEVE	0	0	1	1
ADASEWE	0	0	4	4
ADASIEVE	3	0	0	3
ADASINE	0	0	1	1
ADASIVE	2	0	6	8
ADASIWE	0	0	6	6
ADASONE	0	0	2	2
ADASOOF	0	1	0	1
ADASUF	0	2	0	2
ADASURE	4	0	3	7
ADASUV	0	1	0	1
ADASUVE	15	1	5	21
ADASWE	0	0	1	1
ADAVASAVE	0	0	1	1
ADDISUFF	0	1	0	1
ADESUF	0	1	0	1
ADISEUS	0	1	0	1
ADISOOF?	0	1	0	1
ADISUF	0	2	0	2
ADISUVE	0	2	0	2

ATASOOF	0	1	0	1
ATASUF	0	1	0	1
ATASUFE	0	1	0	1
ATASUV	0	1	0	1
ATISOOF	0	1	0	1
ATISUF	0	2	0	2
ATISUSE	0	1	0	1
ATISUV	0	1	0	1
ATISUVE	0	1	0	1
ATOSOOF	0	1	0	1
ATTISUSE	0	1	0	1

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

No.	Product Name	Similarity to Adasuve	Failure preventions
1.	Aleve (Naproxen)	Look	The pair have sufficient orthographic differences.
2.	Acanya (Clindamycin Phosphate and Benzoyl Peroxide)		The pair have sufficient orthographic differences.
3.	Ablavar (Gasofosveset Trisodium)	Look	The pair have sufficient orthographic differences.
4.	Sitavig*** (Acyclovir Lauriad)	Look	The pair have sufficient orthographic differences.
5.	Albenza (Albendazole)	Look	The pair have sufficient orthographic differences.
6.	(b) (4)	Look	(b) (4)
7.	Aclamen	Look	The trademark for this name is owned by GlaxoSmithKline according to USPTO. However, unable to identify a drug with this name. Additionally, this name is not on the DMEPA proprietary name consultation requests list.

No.	Product Name	Similarity to Adasuve	Failure preventions
8.	Actemra (Tocilizumab)	Look	The pair have sufficient orthographic differences.
9.	Acticin (Permethrin)	Look	The pair have sufficient orthographic differences.
10.	Abreva (Docosanol)	Look	The pair have sufficient orthographic differences.
11.	Achara also known as Lemongrass	Look	This is a botanical and not a drug product.
12.	Ultrase (Amylase, Lipase, and Protease)	Look	The pair have sufficient orthographic differences.
13.	Alinia (Nitazoxanide)	Look	The pair have sufficient orthographic differences.
14.	Altabax (Retapamulin)	Look	The pair have sufficient orthographic differences.
15.	Atorvastatin	Look	The pair have sufficient orthographic differences.
16.	Pediasure	Look	The pair have sufficient orthographic differences.
17.	Ativan (Lorazepam)	Look	The pair have sufficient orthographic differences.
18.	Antara (Fenofibrate)	Look	The pair have sufficient orthographic differences.
19.	Adalat (Nifedipine)	Look	The pair have sufficient orthographic differences.
20.	Adefovir	Look	The pair have sufficient orthographic differences.
21.	AdreView (Iobenguane Sulfate I 123)	Look	The pair have sufficient orthographic differences.
22.	Antabuse (Disulfiram)	Look	The pair have sufficient orthographic differences.
23.	Adoxa (Doxycycline Monohydrate)	Look	The pair have sufficient orthographic differences.
24.	Alteplase	Look	The pair have sufficient orthographic differences.
25.	Atropine	Look	The pair have sufficient orthographic differences.
26.	Actonel (Risedronate Sodium)	Look	The pair have sufficient orthographic differences.

No.	Product Name	Similarity to Adasuve	Failure preventions
27.	Adagen (Pegademase Bovine)	Look	The pair have sufficient orthographic differences.
28.	Advair (Fluticasone Propionate and Salmeterol)	Look	The pair have sufficient orthographic differences.
29.	Adderall (Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate)	Look	The pair have sufficient orthographic differences.
30.	Atarax (Hydroxyzine Hydrochloride)	Look	The pair have sufficient orthographic differences.
31.	Aldomet (Methyldopa)	Look	The pair have sufficient orthographic differences.
32.	Advil (Ibuprofen)	Look	The pair have sufficient orthographic differences.
33.	Avastin (Bevacizumab)	Look	The pair have sufficient orthographic differences.
34.	Aclaro (Hydroquinone)	Look	The pair have sufficient orthographic differences.
35.	Ciclesonide	Look	The pair have sufficient orthographic differences.
36.	Cida-Stat (Chlorhexidine)	Look	The pair have sufficient orthographic differences.
37.	Adapin (Doxepin Hydrochloride)	Look	The pair have sufficient orthographic differences.
38.	Amidate (Etomidate)		
39.	(b) (4)	Look	(b) (4)
40.	(b) (4)	Look	(b) (4)
41.	Adagin (Calcium 36 mg, Proprietary Blend 520 mg, L-Arginine, Mucuna Pruriens 15% L-Dopa, Ashwaganda, Alpha GPC, Tribulis Terrestris, Extract 40%, Cordyceps Sinensis Extract, Optizine)	Look	This natural product has been discontinued.

No.	Product Name	Similarity to Adasuve	Failure preventions
42.	Actanol	Look	This name was found in Facts and Comparisons Online, however, no product characteristics were provided. Unable to locate product characteristics in our usual databases.
43.	Actical (Calcium, Magnesium, Phytonadione, Vitamin D)	Look	The pair have sufficient orthographic differences.
44.	Adocaine (Cod Liver Oil, Dipiperdon HCl, Vitamin A, Vitamin D, and Zinc Oxide)	Look	This name was found in Micromedex. The product ingredients were listed but there was no dosage information specific to this product available. Product information not available in our usual databases.

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.

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
1.	Abraxane (Paclitaxel) for Injection, 100 mg <u>Usual Dose</u> 260 mg/m ² intravenously over 30 minutes every 3 weeks.	<u>Orthographic</u> Both names start with the letter 'A', contain letter 'a' in the middle of the names, and contain one upstroke. Additionally, the letter string 'uve' in Adasuve may appear similar to the letter string 'ane' in Abraxane when scripted.	<u>Orthographic:</u> The letters "br" in Abraxane do not look like the letter "d" in Adasuve. Additionally, the letter "x" in Abraxane does not look like the letter "s" in Adasuve. <u>Dose</u> 10 mg vs. 260 mg/m ² There is no overlap in doses of the products.

No.	Proposed name: Adasuve (Lorazepam) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
2.	Cidofovir Injection, 375 mg/5 mL (75 mg/mL) <u>Usual Dose</u> 5 mg/kg body weight as intravenous infusion over 1 hour administered once every 2 weeks.	<u>Orthographic</u> The letter strings ‘ada’ and ‘uve’ in Adasuve appear similar to the corresponding letter strings ‘ciclo’ and ‘ovi’ in Cidofovir when scripted if the first letters of the names are scripted in a lower case.	<u>Orthographic</u> The name Cidofovir contains a down stroke whereas Adasuve does not. <u>Dose</u> 10 mg vs. 5 mg/kg The products do not have overlapping doses.
3.	Udamin (Multivitamin) Caplet Udamin SP (Multivitamin) Caplet <u>Usual Dose</u> Take 1 caplet daily	<u>Orthographic</u> Both names contain 1 upstroke. Additionally, the letter string ‘adasu’ may appear similar to the corresponding letter string ‘udam’ when scripted. <u>Similar dose</u> 1 inhalation vs. 1 caplet	<u>Settings of Use</u> Under direct supervision of HCP in ER or psychiatric facility during acute agitation vs. by prescription in outpatient and inpatient settings for non-emergency.
4.	Adcetris (Brentuximab Vedotin) Powder for Injection, 50 mg per vial <u>Usual Dose</u> 1.8 mg/kg intravenously over 30 minutes every 3 weeks for a maximum of 16 cycles.	<u>Orthographic</u> The letter string ‘Ada’ may appear similar to the corresponding letter string ‘Adce in Adcetris when scripted. <u>Dose:</u> The potential exists for numerical overlap between the doses of the products (10 mg vs. 100 mg)	<u>Orthographic</u> The suffixes “suve” vs. “tris” do not look similar. <u>Route of administration:</u> Adcetris is a chemotherapeutic agent so it is likely the route of administration and duration of infusion would be specified on an order.

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
5.	<p>Advicor (Niacin and Lovastatin) Tablets, 500 mg/20 mg, 750 mg/20 mg, 1000 mg/20 mg, 1000 mg/40 mg</p> <p><u>Usual Dose</u> 500 mg/20 mg to 1000 mg/20 mg orally once to twice daily and 1000 mg/40 mg orally once daily</p>	<p><u>Orthographic</u> Both names start with the letter string ‘Ad’. Additionally, the letter string ‘uv’ in Adasuve may appear similar to the corresponding letter string ‘or’ in Advicor when scripted.</p>	<p><u>Orthographic</u> The letter string ‘as’ in Adasuve lacks orthographic similarity to the corresponding letter string ‘vic’ in Advicor.</p> <p><u>Strength</u> 10 mg vs. multiple strengths.</p> <p>The strength of Advicor must be specified and none of the strengths overlap with Adasuve.</p>
6.	<p>Advera Liquid Nutrition (Multivitamin) Liquid</p> <p><u>Usual Dose</u> Based upon individual need under medical supervision</p>	<p><u>Orthographic</u> Both names start with the letter string ‘Ad’. Additionally, the letter string ‘su’ in Adasuve may appear similar to the corresponding letter string ‘ra’ in Advera when scripted.</p>	<p><u>Orthographic</u> The name Adasuve appears longer in length when written as compared to Advera. Additionally, the suffixes “suve” vs. “vera” look different.</p> <p><u>Dosage Units:</u> mg vs. mL</p> <p><u>Context of use:</u> Under direct supervision of HCP in ER or psychiatric facility during acute agitation vs. a nutritional supplement that would not be used in an emergency setting.</p>
7.	<p>Alvesco (Ciclesonide) Inhalation Solution, 80 mcg per actuation and 160 mcg per actuation</p> <p><u>Usual Dose</u> 80 mcg to 160 mcg by oral inhalation twice daily</p>	<p><u>Orthographic</u> Both names start with the letter ‘A’ and contain an upstroke letter in the second position.</p> <p><u>Route of Administration</u> Oral Inhalation</p>	<p><u>Orthographic:</u> The suffixes “asuve” vs. “vesco” look different when written.</p> <p><u>Strength</u> 10 mg vs. 80 mcg or 160 mcg per actuation.</p> <p>There is no overlap in strength between the products.</p>

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
8.	<p>Azasan (Azathioprine) Tablets 75 mg and 100 mg</p> <p><u>Usual Dose</u> Starting dose: 3 mg/kg to 5 mg /kg as a single dose on the day of transplantation. Maintenance dose 1 mg/kg to 3 mg/kg once daily.</p>	<p><u>Orthographic</u> Both names start with the letter 'A'. Additionally, the letter string 'asuve' may appear similar to the corresponding letter string 'asan' when scripted.</p> <p><u>Strength:</u> There is numerical overlap between the product strengths (10 mg vs. 100 mg)</p>	<p><u>Orthographic</u> The name Adasuve contains 2 upstrokes vs. the name Azasan contains 1 upstroke and 1 down stroke if the letter 'z' is scripted as a down stroke. Additionally, the letter 'd' in Adasuve lacks orthographic similarity to the letter 'z' in Azasan.</p>
9.	<p>Aldara (Imiquimod) Topical Cream, 5%</p> <p><u>Usual Dose</u> Apply to affected area once daily three times a week just prior to sleep.</p>	<p><u>Orthographic</u> Both names start with the letter 'A' and the letter string 'dasu' in Adasuve may appear similar to the letter string 'dara' in Aldara when scripted.</p>	<p><u>Orthographic</u> The beginning letter "A" in Aldara of followed by an upstroke letter whereas the letter "A" in Adasuve is not.</p> <p><u>Frequency of Administration</u> One time vs. three times a week</p>

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
10.	<p>Stalevo (Carbidopa, Levodopa, and Entacapone) Tablets, 12.5 mg/50 mg/200 mg, 18.75 mg/75 mg/200 mg, 25 mg/100 mg/200 mg, 31.25 mg/125 mg/200 mg, 37.5 mg/150 mg/200 mg, 50 mg/200 mg/200 mg</p> <p><u>Usual Dose</u> 12.5 mg/50 mg/200 mg to 37.5 mg/150 mg/200 mg eight tablets daily in one or more divided doses. 50 mg/200mg/200mg six tablets daily in one or more divided doses.</p>	<p><u>Orthographic</u> The letter string 'Ada' may appear similar to the corresponding letter string 'Sta' when scripted.</p>	<p><u>Orthographic</u> The name Adasuve contains 2 upstrokes vs. the name Stalevo contains 3 upstrokes. Additionally, the letter string 'su' in Adasuve lacks orthographic similarity to the corresponding letter string 'le' in Stalevo when scripted.</p> <p><u>Strength</u> 10 mg vs. multiple strengths.</p> <p>The strength of Stalevo must be specified. The products do not overlap in strength.</p>
11.	<p>Stavzor (Valproic Acid) Delayed-release Capsule, 125 mg, 250 mg, and 500 mg</p> <p><u>Usual Dose</u> Mania: 750 mg daily in divided doses Epilepsy: 10 mg/kg to 15 mg/kg per day up to 60 mg/kg per day can be administered in divided doses.</p>	<p><u>Orthographic</u> Both names contain 1 upstroke. Additionally, the letter string 'Adas' and the letter 'v' in Adasuve may appear similar to the corresponding letter string 'Stav' and the letter 'r' when scripted.</p>	<p><u>Strength</u> 10 mg vs. multiple strengths</p> <p>The products do not overlap in strength.</p> <p><u>Dose:</u> 10 mg vs. 10 mg/kg/day to 60 mg/kg/day The products do not have overlapping doses</p> <p><u>Frequency of Administration</u> One time vs. once daily to several times daily.</p>

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
12.	<p>Alcaine (Proparacaine) Ophthalmic Solution, 0.5%</p> <p><u>Usual Dose</u> For ophthalmic anesthesia: •for tonometry: Instill 1 or 2 drops into eye(s) immediately before measurement. •for foreign body removal: Instill 1 or 2 drops into eye(s) prior to procedure. •for suture removal: Instill 1 or 2 drops into eye(s) 2 to 3 minutes prior to suture removal. •in deeper procedures such as cataract extraction: instill 1 drop into eye(s) every 5 to 10 minutes for 5 to 7 doses.</p>	<p><u>Orthographic</u> Both names contain 2 upstrokes and no down strokes. Additionally, Both names start with the letter 'A' and contain the letter 'a' in the middle of the names. Furthermore, the letter string 've' in Adasuve may appear similar to the letter string 'ne' in Alcaine when scripted.</p>	<p><u>Settings of Use</u> Under direct supervision of HCP in ER or psychiatric facility during acute agitation vs. in ophthalmologist office during a specific procedure performed.</p>
13.	(b) (4)		

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
14.	Adcirca (Tadalafil) Tablets 20 mg <u>Usual dose:</u> 40 mg orally once daily	<u>Orthographic:</u> Both names begin with “Ad” and the letters “ci” may look like the letter “a”.	<u>Orthographic:</u> The ending letters (“rca” vs. “suve”) look different. <u>Dose:</u> 10 mg vs. 40 mg The products do not have overlapping doses.
15.	Aclovate (Aclometasone Dipropionate) Cream and Ointment 0.05% <u>Dose:</u> Apply a thin film to the affected skin areas twice daily; three times per day	<u>Orthographic:</u> The beginning letters in the names look similar (“Ada” vs. “Aclo”). <u>Strength:</u> Both products are available in a single strength so the strength does not have to be specified on a prescription.	<u>Orthographic:</u> Aclovate contains the upstroke and cross-stroke letter “t” whereas Adasuve does not. <u>Frequency of administration:</u> Once vs. twice daily or three times per day
16.	Absorica (Isotretinoin) Capsules 10 mg, 20 mg, 30 mg, and 40 mg <u>Usual Dosage:</u> 10 mg to 100 mg orally twice daily	<u>Orthographic:</u> Both names begin with the letter “A”. The letter strings “suve” vs. “sori” may look similar when written. <u>Strength:</u> Both products are available in a 10 mg strength.	<u>Orthographic:</u> The third position letters “a” vs. “s” do not look similar. The ending letters “ca” in Absorica do not look similar to the ending letters “ve” in Adasuve. <u>Frequency of administration:</u> One time vs. twice daily <u>Context of use:</u> Both products have a REMS and there are specific requirements for obtaining these products. Adasuve must only be administered by a HCP and administered in a facility where resuscitation equipment is available.

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
17.	<p>Activase (Alteplase) Powder for Reconstitution 50 mg and 100 mg</p> <p>Dosage: 0.9 mg/kg, maximum of 90 mg;</p> <p>15 mg bolus, then 50 mg over 30 min., then 35 mg over 60 min.</p> <p>15 mg bolus then 0.75 mg/kg (max. 50 mg) over 30 min. then 0.5 mg/kg (max. 35 mg) over 60 min.</p> <p>100 mg over 2 hours</p>	<p><u>Orthographic:</u> Both names begin with the letter “A”. The suffixes “suve” vs. “vase” may look similar when written because they do not contain any upstroke, downstroke, or cross stroke characteristics.</p> <p><u>Dose:</u> The products have numerical similarity in dose (10 mg vs. 100 mg)</p>	<p><u>Orthographic:</u> Activase contains the upstroke letter “t” whereas Adasuve does not.</p> <p><u>Route of administration:</u> Oral inhalation vs. intravenous bolus or infusion</p>
18.	<p>Alsuma (Sumatriptan) Injection 6 mg/0.5 mL</p> <p><u>Usual dosage:</u> 6 mg once, may repeat after 1 hour. Do not exceed 12 mg per 24 hours</p>	<p><u>Orthographic:</u> Both names begin with the letter “A” and contain an upstroke letter in the second position. The ending letters “suve” vs. “suma” may look similar when written.</p> <p><u>Strength:</u> Both products are available in a single strength which can be omitted from a prescription.</p>	<p><u>Orthographic:</u> The infixes “asuv” vs. “sum” look different.</p> <p><u>Dose:</u> 10 mg vs. 6 mg The products do not have overlapping doses.</p>

No.	Proposed name: Adasuve (Lorapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
19.	Alavert (Loratidine) Tablets and Orally Disintegrating Tablets, 10 mg <u>Usual Dosage:</u> 10 mg orally once daily OTC Product	<u>Orthographic:</u> Both names begin with the letter “A”; contain an upstroke letter in the second position and the letter “a” in the third position. <u>Strength and dose:</u> Both products overlap in strength (10 mg) and dose (10 mg). Both products are available in a single strength which could be omitted on a prescription.	<u>Orthographic:</u> The suffixes (“suve” vs. “vert” look different when written. Additionally, the upstroke and cross-stroke letter “t” in Alavert helps to differentiate the names.
20.	Aluvea (Urea) Cream 39% <u>Dosage:</u> Apply to affected skin twice daily	<u>Orthographic:</u> Both names begin with the letter “A”; contain an upstroke letter in the second position. The third position letters “a” vs. “u” may look similar when written. Both products are available in a single strength which could be omitted on a prescription.	<u>Orthographic:</u> Adasuve appears longer in length when written. <u>Frequency of administration:</u> One time vs. twice daily
21.	Atacand (Candesartan) Tablets 4 mg, 8 mg, 16 mg, and 32 mg <u>Dosage:</u> 4 mg to 32 mg orally once daily	<u>Orthographic:</u> Both names begin with the letter “A”; contain an upstroke letter in the second position and the letter “a” in the third position.	<u>Orthographic:</u> The suffixes (“suve” vs. “cand”) look different. Additionally, the upstroke letter “d” in Atacand helps to differentiate the names. <u>Strength:</u> 10 mg vs. multiple strengths The products do not overlap in strength.

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
22.	Adacel (Diphtheria Toxoid/Tetanus Toxoid/Acellular Pertussis Vaccine, Adsorbed) <u>Dosage:</u> 0.5 mL intramuscularly, once	<u>Orthographic:</u> Both names begin with the letters “Ada”. <u>Frequency of administration:</u> Both products are administered once.	<u>Orthographic:</u> The suffixes “suve” vs. “cel” do not look similar.
23.	Abacavir Sulfate Tablets and Oral Solution Tablets: 300 mg Oral Solution: 20 mg/mL <u>Usual Dosage:</u> <i>Adults:</i> 600 mg once daily; 300 mg twice daily <i>Children:</i> 8 mg/kg twice daily up to 300 mg twice daily <i>Mild hepatic impairment:</i> 200 mg twice daily	<u>Orthographic:</u> The beginning letters “Ada” vs. “Aba” may look similar when written. <u>Dose:</u> The potential exists for numerical similarity between the doses (10 mg vs. 100 mg)	<u>Orthographic:</u> The suffixes “suve” vs. “cavir” look different.

No.	Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength: 10 mg	Usual dosage: 10 mg by oral inhalation, using a single use inhaler; administer only a single dose within any 24-hour period.
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
24.	<p>Adenosine Injection</p> <p><u>Strengths:</u> 3 mg/mL</p> <p><u>Usual Dosage:</u> <i>Treatment</i> Initial dosage: 6 mg given as a rapid IV bolus</p> <p>Repeat administration: If the first dose does not result in elimination of the SVT within 1 to 2 minutes, give 12 mg. Repeat the 12 mg dose a second time if required. Doses of more than 12 mg are not recommended</p> <p>Children less than 50 kg: 0.05 to 0.1 mg/kg as a rapid IV bolus</p> <p><i>Diagnostic aid:</i> 140 mcg/kg/min infused for 6 minutes (total dose of 0.84 mg/kg)</p>	<p><u>Orthographic:</u> Both names begin with the letters “Ad”. The suffixes “suve” vs. “sine” look similar when written.</p> <p><u>Frequency of administration:</u> Both products can be administered one time.</p>	<p><u>Orthographic:</u> Adenosine appears longer in length (9 letters) as compared to Adasuve (7 letters) when written. Additionally, the infix letters “a” vs. “eno” do not look similar.</p> <p><u>Dose:</u> 10 mg vs. 6 mg, 12 mg or 0.05 to 0.1 mg/kg for patients less than 50 kg</p>

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

/s/

LORETTA HOLMES
10/05/2012

IRENE Z CHAN
10/05/2012

CAROL A HOLQUIST
10/05/2012

**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: April 12, 2012

Reviewer: Yelena Maslov, Pharm.D., Acting Team Leader
Division of Medication Error Prevention and Analysis

Drug Name and Strengths: Adasuve (Loxapine) Inhalation Powder, 5 mg and 10 mg

Application Type/Number: NDA 022549

Applicant/sponsor: Alexza Pharmaceuticals, Inc.

OSE RCM #: 2012-446

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

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Adasuve, 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, Adasuve, acceptable in OSE Review #2011-4069, dated January 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 #2011-4069. 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 Adasuve and represent a potential source of drug name confusion. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with (b) (4) and lead to medication errors. This analysis determined that the name similarity between Adasuve 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 April 2, 2012. The Office of Prescription Drug Promotion (OPDP) re-reviewed the proposed name on March 1, 2012 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Adasuve, did not identify any vulnerabilities that would result in medication errors with any additional name(s) noted in this review. Thus, DMEPA has no objection to the proprietary name, Adasuve, 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 Psychiatry Products (DPP) 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 Sandra Griffith, OSE project manager, at 301-796-2445.

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

4 REFERENCES

1. *Maslov, Yelena, OSE Review #2011-4069. Proposed Proprietary Name Review for Adasuve, January 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.

Appendix A: FMEA Table

Proposed name, strengths, and usual dose: Adasuve (Loxapine) Inhalation Powder, 5 mg to 10 mg Inhale once as directed by healthcare provider	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion: Causes (could be multiple)	Prevention of Failure Mode
(b) (4)		

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

/s/

YELENA L MASLOV
04/02/2012

**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: January 12, 2011

Reviewer: Yelena Maslov, Pharm.D., Safety Evaluator
Division of Medication Error Prevention and Analysis

Team Leader Irene Z. Chan, Pharm.D., BCPS, Team Leader
Division of Medication Error Prevention and Analysis

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

Drug Name(s) and Strength: Adasuve (Loxapine) Inhalation Powder, 5 mg and 10 mg

Application Type/Number: NDA 022549

Applicant/Sponsor: Alexza Pharmaceuticals, Inc.

OSE RCM #: 2011-4069

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Adasuve, 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.

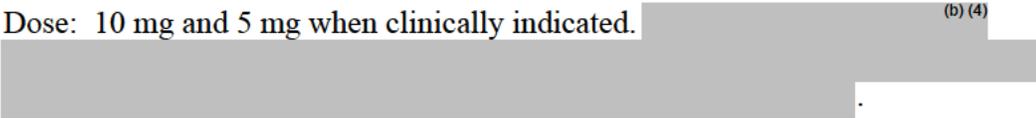
1.1 REGULATORY HISTORY

This review responds to a request from Alexza Pharmaceuticals, Inc., dated October 25, 2011, for a re-assessment of the proposed proprietary name, Adasuve, regarding potential name confusion with other proprietary or established drug names in the usual practice setting. The proposed proprietary name was previously found acceptable on May 6, 2010 in OSE Review #2010-371.

The product received a Complete Response on October 8, 2010. The Applicant submitted a response to a complete response for Adasuve on August 4, 2011.

1.2 PRODUCT INFORMATION

The following product information is provided in the October 25, 2011, proprietary name submission.

- Established Name: Loxapine
- Indication of Use: Rapid treatment of agitation associated with schizophrenia or bipolar disorder in adults
- Route of administration: oral inhalation
- Strength: 5 mg and 10 mg
- Dosage form: Inhalation Powder
- Dose: 10 mg and 5 mg when clinically indicated. (b) (4)

- How Supplied: in Single-use disposable inhalers containing 5 mg or 10 mg of Loxapine Inhalation Powder. Each inhaler is provided in a sealed foil pouch. Each carton contains 5 foil pouches.
- Storage: 15° to 30°C (59° to 86°F)
- Container and Closure systems: Each inhaler is provided in a sealed foil pouch. Each carton contains 5 foil pouches.

The product will have an extensive REMS program with ETASU due to pulmonary toxicity and bronchospasm concerns. Although the program is not yet finalized, it is likely that the healthcare institution and prescribers will be registered in order to prescribe and dispense the medication. Additionally, this product will only be available in healthcare institutions that are able to deliver rescue treatment (e.g., intubation, ventilators, short-acting beta agonist inhalers) to a patient that develops bronchospasm.

2 RESULTS

The following sections provide the information obtained and considered in the 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 and the Division of Psychiatric Products (DPP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

On December 6, 2011, the United States Adopted Name (USAN) stem search identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide derivation of the proprietary name. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Thirty-three practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Eight participants interpreted the proposed proprietary name correctly as 'Adasuve' with seven correct interpretations occurring with outpatient orders and one correct interpretation occurring with voice orders. The remaining 25 participants misinterpreted the name Adasuve. The most common misinterpretation occurred with the letter 'v' as the letter 'r'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, November 4, 2011, e-mail, DPP did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 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, Adasuve. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Adasuve, 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)

<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Aleve	EPD	Aclamen	EPD	Adcetris	EPD
Acanya	EPD	Abraxane	EPD	Advicor	EPD
Ablavar	EPD	Ciclesonide	EPD	Advera	EPD
Albenza	EPD	Cidofovir	EPD	Alvesco	EPD
Sitavig ^{***}	EPD	Udamin	EPD	Azasan	EPD
(b) (4)	EPD	Aclaro	EPD	Aldara	EPD
Stalevo	EPD	Stavzor	EPD	Alcaine	EPD
Sound Similar					
None identified					
Look and Sound Similar					
None identified					

Our analysis of the 21 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined all 21 names will not pose a risk for confusion as described in Appendix D through E.

2.2.6 Communication of DMEPA’s Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Psychiatry Products (DPP) via e-mail on December 6, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DPP on December 9, 2011, no additional concerns were noted with the proposed proprietary name, Adasuve.

3 CONCLUSIONS

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

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Adasuve, and have concluded that this name is acceptable. If the approval of the proposed proprietary name is delayed beyond 90 day period after completion of this review, the proprietary name must be re-reviewed. However, if any of the proposed product characteristics as stated in

^{***} This document contains proprietary information that should not be released to the public

your October 25, 2011, submission are altered prior to approval of the marketing application, DMEPA rescinds this finding and the name must be resubmitted for review.

4 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. 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.

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. ***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 Pharmacy's Fundamental Reference**

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.

15. **Medical Abbreviations Book**

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

16. **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.

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 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.

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

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 product characteristics considered for this review appears in Appendix B1 of this review.

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.).

2. 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 Division of Drug Marketing, Advertising, and Communications (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.

3. 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.

4. 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.

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, 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 Appendix B1 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

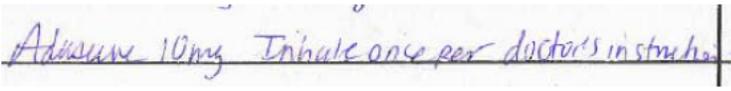
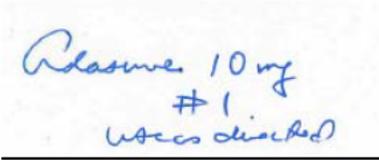
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency’s credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors’ have changed a product’s proprietary name in the post-approval 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, Adasuve	Scripted May Appear as	Spoken May Be Interpreted as
Capital Letter ‘A’	‘O’, ‘S’, ‘D’, ‘C’	Any vowel
Lower case ‘a’	‘E’, ‘c’, ‘d’, ‘o’, ‘u’, ‘n’	Any vowel
Lower case ‘d’	‘el’, ‘cl’, ‘f’, ‘t’	‘t’
Lower case ‘s’	‘v’, ‘r’, ‘c’, ‘g’	‘x’, ‘z’
Lower case ‘u’	‘a’, ‘n’, ‘v’	Any vowel
Lower case ‘v’	‘r’, ‘u’, ‘n’, ‘w’, ‘k’, ‘z’	‘w’, ‘z’, ‘b’, ‘th’
Lower case ‘e’	‘a’, ‘c’, ‘i’, ‘l’, ‘o’	Any vowel

Appendix C: Prescription Simulation Samples and Results

Figure 1. Adasuve Study (Conducted on 11/14/2011)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Adasuve 10 mg #1 Use as directed</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (n=33)

INPATIENT	VOICE	OUTPATIENT
ADUSUNE	ADASOOTH	ADASERVE
ADUSUNE	ADASUVE	ADASERVE
ADUSURE	ADESUF	ADASINE
ADUSURE	ADISOO THE	ADASIVE
ADUSURE	ADISUVE	ADASURE
ADUSUVE	ADISUVE	ADASURE
ADUSURE	ATASUZ	ADASURVE
	ATICUV	ADASUVA
	ATISOO TH	ADASUVE
	ATTASUS	ADASUVE
	ATTISUV	ADASUVE
		ADASUVE

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

Product Name	Similarity to Adasuve	Failure preventions
Aleve (Naproxen)	Looks alike	Lacks convincing orthographic similarity
Acanya (Clindamycin Phosphate and Benzoyl Peroxide)	Looks alike	Lacks convincing orthographic similarity
Ablavar (Gadofosveset Trisodium)	Looks alike	Lacks convincing orthographic similarity
Albenza (Albendazole)	Looks alike	Lacks convincing orthographic similarity
Sitavig*** (Acyclovir Lauriad)	Looks alike	Lacks convincing orthographic similarity
(b) (4)	Looks alike	(b) (4)
Aclamen	Looks alike	The trademark appears registered in Saegis and USPTO. However, no product characteristics are available from any other database in Reference Section 4. Additionally, it appears that the trademark is registered without a proposed product.

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

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.

Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength(s): 5 mg and 10 mg	Usual dose: Inhale once as directed by the healthcare provider
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
<p>Abraxane (Paclitaxel) for Injection, 100 mg</p> <p><u>Usual Dose</u> 260 mg/m² intravenously over 30 minutes every 3 weeks.</p>	<p><u>Orthographic</u> Both names start with the letter ‘A’, contain letter ‘a’ in the middle of the names, and contain one upstroke. Additionally, the letter string ‘uve’ in Adasuve may appear similar to the letter string ‘ane’ in Abraxane when scripted.</p>	<p><u>Strength</u> Multiple strengths vs. single strength and no overlap in strength. Thus, Adasuve’s strength will be specified vs. Abraxane’s strength may be omitted.</p> <p><u>Dose</u> No overlap in doses of the product and doses must be specified because Adasuve can be dosed at 5 mg or 10 mg and Abraxane is dose is based on body surface area (BSA).</p>
<p>Ciclesonide Inhalation Solution, 80 mcg per actuation and 160 mcg per actuation</p> <p><u>Usual Dose</u> 80 mcg to 160 mcg by oral inhalation twice daily</p> <p>Ciclesonide Nasal Spray, 50 mcg per actuation</p> <p><u>Usual Dose</u> 2 sprays to each nostril once daily.</p>	<p><u>Orthographic</u> The letter strings ‘ad’ and ‘suv’ in Adasuve may appear similar to the corresponding letter strings ‘cicl’ and ‘son’ in Ciclesonide when scripted if the first letters of the names are scripted in a lower case.</p> <p><u>Route of Administration</u> Oral Inhalation</p>	<p><u>Orthographic</u> The name Adasuve contains 2 upstrokes and the name Ciclesonide contains 3 upstrokes. Additionally, the name Ciclesonide is longer than Adasuve (11 letters vs. 7 letters)</p> <p><u>Strength</u> Both products are available in multiple strengths, so the strength must be specified. There is no overlap in strength between the products.</p>

Proposed name: Adasuve (Lorazepam) Inhalation Powder	Strength(s): 5 mg and 10 mg	Usual dose: Inhale once as directed by the healthcare provider
<p>Cidofovir Injection, 375 mg/5 mL (75 mg/mL)</p> <p><u>Usual Dose</u> 5 mg/kg body weight as intravenous infusion over 1 hour administered once every 2 weeks.</p>	<p><u>Orthographic</u> The letter strings ‘ada’ and ‘uve’ in Adasuve appear similar to the corresponding letter strings ‘ciclo’ and ‘ovi’ in Cidofovir when scripted if the first letters of the names are scripted in a lower case.</p>	<p><u>Orthographic</u> The name Cidofovir contains a down stroke vs. the name Adasuve does not.</p> <p><u>Strength</u> Multiple strengths vs. single strength and no overlap in strength. Thus, Adasuve’s strength will be specified vs. Cidofovir’s strength may be omitted.</p> <p><u>Dose</u> The doses for both products must be specified. Cidofovir’s dose must be specified based on mg/kg. No dose overlap.</p>
<p>Udamin (Multivitamin) Caplet</p> <p>Udamin SP (Multivitamin) Caplet</p> <p><u>Usual Dose</u> Take 1 caplet one daily</p>	<p><u>Orthographic</u> Both names contain 1 upstroke. Additionally, the letter string ‘adasu’ may appear similar to the corresponding letter string ‘udam’ when scripted if the first letters of the names are scripted in a lower case.</p> <p><u>Similar dose</u> 1 caplet vs. 1 tablet</p>	<p><u>Strength</u> Multiple strengths vs. single strength and no overlap in strength. Thus, Adasuve’s strength will be specified vs. Udamin’s strength may be omitted.</p> <p><u>Settings of Use</u> Under direct supervision of HCP in ER or psychiatric facility during acute agitation vs. by prescription in outpatient and inpatient settings.</p>
<p>Aclaro (Hydroquinone)Topical Emulsion, 4%</p> <p>Aclaro PD (Hydroquinone)Topical Emulsion, 4%</p> <p><u>Usual Dose</u> Apply to affected area twice daily</p>	<p><u>Orthographic</u> The letter string ‘Adasu’ may appear similar to the corresponding name Aclaro when scripted</p>	<p><u>Orthographic</u> The name Adasuve appears longer than the name Aclaro.</p> <p><u>Strength</u> Multiple strengths vs. single strength and no overlap in strength. Thus, Adasuve’s strength will be specified vs. Aclaro’s strength may be omitted.</p> <p><u>Frequency of Administration</u> One time vs. twice daily</p>

Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength(s): 5 mg and 10 mg	Usual dose: Inhale once as directed by the healthcare provider
<p>Adcetris (Brentuximab) Powder for Injection, 50 mg per vial</p> <p><u>Usual Dose</u> 1.8 mg/kg intravenously over 30 minutes every 3 weeks for a maximum of 16 cycles.</p>	<p><u>Orthographic</u> The letter string ‘Ada’ and the letter ‘u’ in Adasuve may appear similar to the corresponding letter strings ‘Adce’ and ‘ri’ in Adcetris when scripted.</p>	<p><u>Orthographic</u> The name Adasuve contains 2 upstrokes vs. the name Adcetris contains 3 upstrokes.</p> <p><u>Strength</u> Multiple strengths vs. single strength and no overlap in strength. Thus, Adasuve’s strength will be specified vs. Adcetris’s strength may be omitted.</p> <p><u>Dose</u> The doses for both products must be specified. No dose overlap. Adcetris’s dose must be specified based on mg/kg.</p>
<p>Advicor (Niacin and Lovastatin) Tablets, 500 mg/20 mg, 750 mg/20 mg, 1000 mg/20 mg, 1000 mg/40 mg</p> <p><u>Usual Dose</u> 500 mg/20 mg to 1000 mg/20 mg orally once to twice daily and 1000 mg/40 mg orally once daily</p>	<p><u>Orthographic</u> Both names start with the letter string ‘Ad’. Additionally, the letter string ‘uv’ in Adasuve may appear similar to the corresponding letter string ‘or’ in Advicor when scripted.</p>	<p><u>Orthographic</u> The letter string ‘as’ in Adasuve lacks orthographic similarity to the corresponding letter string ‘vic’ in Advicor.</p> <p><u>Strength</u> Both products are available in multiple strengths, so the strength must be specified. There is no overlap in strength between the products.</p> <p><u>Dose</u> No overlap in strength or dose. Since multiple strengths are available for both products, dose must be specified.</p>

Proposed name: Adasuve (Loxapine) Inhalation Powder	Strength(s): 5 mg and 10 mg	Usual dose: Inhale once as directed by the healthcare provider
<p>Advera Liquid Nutrition (Multivitamin) Liquid</p> <p><u>Usual Dose</u> Based upon individual need under medical supervision</p>	<p><u>Orthographic</u> Both names start with the letter string 'Ad'. Additionally, the letter string 'su' in Adasuve may appear similar to the corresponding letter string 'ra' in Advera when scripted.</p>	<p><u>Orthographic</u> The name Adasuve appears longer than the name Advera due to winder letter 'a' and the number of letters (7 letters vs. 6 letters). Additionally, the letter 'a' in Adasuve lacks orthographic similarity to the letter string 've' in Advera.</p> <p><u>Strength</u> Multiple strengths vs. single strength and no overlap in strength. Thus, Adasuve's strength will be specified vs. Advera's strength may be omitted.</p>
<p>Alvesco (Ciclesonide) Inhalation Solution, 80 mcg per actuation and 160 mcg per actuation</p> <p><u>Usual Dose</u> 80 mcg to 160 mcg by oral inhalation twice daily</p>	<p><u>Orthographic</u> Both names start with the letter 'A' and contain 1 upstroke. Additionally, the letter string 'su' in Adasuve may appear similar to the corresponding letter string 'sco' in Alvesco when scripted.</p> <p><u>Route of Administration</u> Oral Inhalation</p>	<p><u>Strength</u> Both products are available in multiple strengths, so the strength must be specified. There is no overlap in strength between the products.</p> <p><u>Dose</u> No overlap in strength or dose. Since multiple strengths are available for both products, dose must be specified.</p> <p><u>Frequency of Administration</u> One time vs. twice daily</p> <p><u>Settings of Use</u> Under direct supervision of HCP in ER or psychiatric facility during acute agitation vs. by prescription</p>
<p>Azasan (Azathioprine) Tablets, 25 mg, 75 mg, 100 mg</p> <p><u>Usual Dose</u> Starting dose: 3 mg/kg to 5 mg/kg as a single dose on the day of transplantation. Maintenance dose 1 mg/kg to 3 mg/kg once daily.</p>	<p><u>Orthographic</u> Both names start with the letter 'A'. Additionally, the letter string 'asuve' may appear similar to the corresponding letter string 'asan' when scripted.</p>	<p><u>Orthographic</u> The name Adasuve contains 2 upstrokes vs. the name Azasan contains 1 upstroke and 1 down stroke if the letter 'z' is scripted as a down stroke. Additionally, the letter 'd' in Adasuve lacks orthographic similarity to the letter 'z' in Azasan.</p> <p><u>Strength</u> Both products are available in multiple strengths, so the strength must be specified. There is no overlap in strength between the products.</p>

<p>Proposed name: Adasuve (Loxapine) Inhalation Powder</p>	<p>Strength(s): 5 mg and 10 mg</p>	<p>Usual dose: Inhale once as directed by the healthcare provider</p>
<p>Aldara (Imiquimod) Topical Cream, 5%</p> <p><u>Usual Dose</u> Apply to affected area once daily three times a week just prior to sleep.</p>	<p><u>Orthographic</u> Both names start with the letter ‘A’ and the letter string ‘dasu’ in Adasuve may appear similar to the letter string ‘dara’ in Aldara when scripted.</p> <p><u>Overlap in Strength and Dose</u> Adasuve can be dosed at the strength of 5 mg vs. Aldara can be dosed at the strength of 5%.</p>	<p><u>Orthographic</u> The name Adasuve contains 2 upstrokes and the name Aldara contains 3 upstrokes.</p> <p><u>Frequency of Administration</u> One time vs. three times a week</p> <p><u>Dose</u> Adasuve’s dose must be specified because it is available in multiple strengths vs. Aldara’s dose may be omitted since it is a single strength product.</p>
<p>Stalevo (Carbidopa, Levodopa, and Entacapone) Tablets, 12.5 mg/50 mg/200 mg, 18.75 mg/75 mg/200 mg, 25 mg/100 mg/200 mg, 31.25 mg/125 mg/200 mg, 37.5 mg/150 mg/200 mg, 50 mg/200 mg/200 mg</p> <p><u>Usual Dose</u> 12.5 mg/50 mg/200 mg to 37.5 mg/150 mg/200 mg eight tablets daily in one or more divided doses. 50 mg/200mg/200mg six tablets daily in one or more divided doses.</p>	<p><u>Orthographic</u> Both names share the letter ‘v’ in similar positions. Additionally, the letter string ‘Ada’ may appear similar to the corresponding letter string ‘Sta’ when scripted.</p>	<p><u>Orthographic</u> The name Adasuve contains 2 upstrokes vs. the name Stalevo contains 3 upstrokes. Additionally, the letter string ‘su’ in Adasuve lacks orthographic similarity to the corresponding letter string ‘le’ in Stalevo when scripted.</p> <p><u>Strength</u> Both products are available in multiple strengths, so the strength must be specified. There is no overlap in strength between the products.</p>

<p>Proposed name: Adasuve (Lorazepam) Inhalation Powder</p>	<p>Strength(s): 5 mg and 10 mg</p>	<p>Usual dose: Inhale once as directed by the healthcare provider</p>
<p>Stavzor (Valproic Acid) Delayed-release Capsule, 125 mg, 250 mg, and 500 mg</p> <p><u>Usual Dose</u> Mania: 750 mg daily in divided doses Epilepsy: 10 mg/kg to 15 mg/kg per day up to 60 mg/kg per day can be administered in divided doses.</p>	<p><u>Orthographic</u> Both names contain 1 upstroke. Additionally, the letter string ‘Adas’ and the letter ‘v’ in Adasuve may appear similar to the corresponding letter string ‘Stav’ and the letter ‘r’ when scripted.</p>	<p><u>Strength</u> Multiple strengths and no overlap in strengths. Thus, the strength for each product must be specified.</p> <p><u>Frequency of Administration</u> One time vs. once daily to several times daily.</p>
<p>Alcaine (Proparacaine) Ophthalmic Solution, 0.5%</p> <p><u>Usual Dose</u> For ophthalmic anesthesia: •for tonometry: Instill 1 or 2 drops into eye(s) immediately before measurement. •for foreign body removal: Instill 1 or 2 drops into eye(s) prior to procedure. •for suture removal: Instill 1 or 2 drops into eye(s) 2 to 3 minutes prior to suture removal. •in deeper procedures such as cataract extraction: instill 1 drop into eye(s) every 5 to 10 minutes for 5 to 7 doses.</p>	<p><u>Orthographic</u> Both names contain 2 upstrokes and no down strokes. Additionally, Both names start with the letter ‘A’ and contain the letter ‘a’ in the middle of the names. Furthermore, the letter string ‘ve’ in Adasuve may appear similar to the letter string ‘ne’ in Alcaine when scripted.</p>	<p><u>Strength</u> Multiple strengths vs. single strength. Thus, Adasuve’s strength will be specified vs. Alcaine’s strength may be omitted.</p> <p><u>Settings of Use</u> Under direct supervision of HCP in ER or psychiatric facility during acute agitation vs. in ophthalmologist office during a specific procedure performed.</p>

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/s/

YELENA L MASLOV
01/12/2012

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01/12/2012



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

Date: May 6, 2010

To: Thomas Laughren, MD, Director
Division of Psychiatry Products

Through: Carlos Mena-Grillasca, RPh, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Judy Park, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name(s): Adasuve (Loxapine) Inhalation Powder
5 mg and 10 mg

Application Type/Number: NDA 022549

Applicant: Alexza Pharmaceuticals, Inc.

OSE RCM #: 2010-371

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EXECUTIVE SUMMARY

Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Our assessment supports the findings of the External Proprietary Name Risk Assessments submitted by the Applicant. Thus, DMEPA finds the proposed proprietary name, Adasuve, acceptable for this product.

The proposed proprietary name must be re-reviewed 90 days before approval of the drug.

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 is written in response to a request from Alexza Pharmaceuticals for assessment of the proposed proprietary name, Adasuve, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

Additionally, container labels and carton labeling were provided for review and comment and will be reviewed in a separate review.

1.2 PRODUCT INFORMATION

Adasuve (Loxapine) Inhalation Powder is indicated for the rapid treatment of agitation associated with Schizophrenia or Bipolar Disorder in adults. The recommended dose is 10 mg (b) (4) via single inhalation. (b) (4)

Adasuve will be available in single-use, disposable units containing either 5 mg or 10 mg of Loxapine. The delivery device's registered name is Staccato®. Adasuve will be packaged in a sealed foil pouches and supplied in a carton of 5 units. The product will be used in a hospital, inpatient or other medically-supervised setting and will be dispensed from a non-retail pharmacy setting.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'A' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{1,2}

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

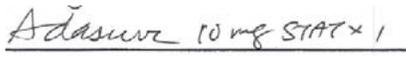
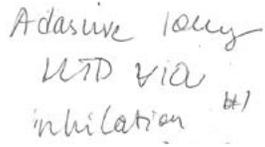
To identify drug names that may look similar to Adasuve, the DMEPA staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (two, capital letter ‘A’ and lower case letter ‘d’); downstrokes (none), cross-strokes (none), and dotted letters (none). Additionally, several letters in Adasuve may be vulnerable to ambiguity when scripted, including the letter ‘A’ may appear as ‘E’, ‘O’, ‘C’, ‘D’, ‘S’, or ‘T’; lower case ‘d’ may appear as ‘cl’ or ‘l’; lower case ‘a’, ‘u’ or ‘e’ may appear as any of the vowels; lower case ‘s’ may appear as ‘c’, ‘g’, ‘n’, ‘r’, or ‘v’; lower case ‘v’ may appear as ‘i’, ‘n’, ‘r’, or ‘s’. As such, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Adasuve.

When searching to identify potential names that may sound similar to Adasuve, DMEPA staff searches for names with similar number of syllables (three), stresses (A-da-suve, a-DA-suve, or a-da-SUVE), and placement of vowel and consonant sounds. Additionally, several letters in Adasuve may be vulnerable to misinterpretation when spoken, including ‘A’ may be interpreted as ‘E’; ‘da’ may be interpreted as ‘ta’ or ‘de’; ‘su’ may be interpreted as ‘soo’ or ‘suh’; and ‘v’ may be interpreted as ‘b’. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Adasuve. The Applicant’s intended pronunciation of the proprietary name (ADD-uh-soov) was taken into consideration. Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Adasuve Rx Study (conducted on March 2, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<u>Inpatient Medication Order :</u> 	Adasuve 10 mg stat x 1
<u>Outpatient Prescription:</u> 	

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

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The database searches yielded a total of 18 names as having some similarity to the name, Adasuve.

Sixteen of the 18 names were thought to look like Adasuve. These names are Aclovate, Cida-stat, Adalat, Adagen, Adapin, (b) (4) Amidate, Adenosine, (b) (4) Adacel, Atacand, Atarax, Adreview, Alamine, Adocaine, and Adagin. The remaining two names (Antabuse and Adcirca) were thought to both look and sound like Adasuve.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 23, 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 Adasuve.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 33 practitioners responded to the prescription analysis studies. One of the practitioners in the verbal study interpreted the name as an existing drug name, Ativan. Therefore, this name will be included as a sound-alike name for evaluation. Twenty seven practitioners in the written study misinterpreted the drug name. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL PROPRIETARY NAME RISK ASSESSMENTS

The Applicant submitted an independent risk assessment of the proposed proprietary name, Adasuve. This study conducted by (b) (4) found the name acceptable. (b) (4) identified and evaluated a total of 18 names for potential confusion with Adasuve. Thirteen of the 18 names were thought to look alike to Adasuve: Adenosine, Atarax, Adacel, Adefovir, Adoxa, Alavert, Aldomet, Altanax, Alteplase, Atorvastatin, Atropine, Avastin, and Pediasure. One of the 18 names (Advil) was thought to sound alike to Adasuve. The remaining four names were thought to look and sound alike to Adasuve: Advair, Adderall, Adalat and Ativan. Of the 18 names, DMEPA also identified four names (Adenosine, Atarax, Adacel and Adalat) during the database searches and one additional name, Ativan, was identified in the prescription studies. The remaining 13 names were added to the Safety Evaluator Assessment: Advair, Adderall, Advil, Adefovir, Adoxa, Alavert, Aldomet, Altanax, Alteplase, Atorvastatin, Atropine, Avastin, Pediasure.

3.5 COMMENTS FROM THE REVIEW DIVISION

3.5.1 Initial Phase of Review

In a response to the OSE March 1, 2010 e-mail, the Division of Psychiatry Products (DPP) did not object to the proposed proprietary name, Adasuve.

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3.5.2 Midpoint of Review

On March 31, 2010, DMEPA notified DPP via e-mail that we had no objections to the proposed proprietary name Adasuve. Per e-mail correspondence from DPP on April 6, 2010, they indicated that they concur with our assessment of the proposed proprietary name, Adasuve.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified two additional names, Adenoscan and Adenocard, thought to look or sound similar to Adasuve and represent a potential source of drug name confusion.

Thus, we identified a total of 34 names for their similarity to the proposed name, Adasuve: 13 identified in the External Study, 1 identified in the prescription analysis studies, 2 identified by the Safety Evaluator, and 18 identified in section 3.1 above.

4 DISCUSSION

This proposed name, Adasuve, 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 Psychiatry Products concurred with the findings of the promotional assessment.

4.2 SAFETY ASSESSMENT

Adasuve is the proposed proprietary name for Loxapine Inhalation Powder. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. DMEPA identified 34 names with potential similarity to the proposed name, Adasuve. No other aspects of the name were identified as a potential source of failures. Eleven names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix C). Additionally, upon further observation, one of the names (Alamine) was found to be a chemical name. Therefore, this name was eliminated from further analysis. Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining 22 names and lead to medication errors. This analysis determined that the name similarity between Adasuve was unlikely to result in medication errors with any of the 22 names for the reasons presented in Appendices D through I.

Thus, DMEPA has no objection to the proprietary name, Adasuve. Our assessment supports the findings of the Proprietary Name Risk Assessment conducted by (b) (4) and submitted by the Applicant.

4.3 PRESENTATION OF THE ESTABLISHED NAME

The established name is presented as “Staccato[®] Loxapine”. However, Staccato[®] is the proprietary name for the inhalation device and should not be part of the established name. DMEPA, ONDQA and Labeling and Nomenclature Committee will meet to discuss the proper designation of the established name and the dosage form. We will address the correct presentation of the established name in the forthcoming labeling review.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Adasuve, is not vulnerable to name confusion that could lead to medication errors nor is it considered promotional.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this NDA is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation. If you have further questions or need clarifications, please contact Sandra Griffith, OSE Project Manager, at 301-796-2445.

5.1 COMMENTS TO THE APPLICANT

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

Adasuve 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 are altered prior to approval of the NDA, 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/category/4782.html>)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.³

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases

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

the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.⁵ DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

Type of similarity	Considerations when searching the databases		
	<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 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, 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

DMEPA requests the Office of New Drugs (OND) responsible for the application for its 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 is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys its decision to accept or reject the name. OND is requested to concur/not concur with DMEPA's final decision.

5. External Proprietary Name Risk Assessment

DMEPA conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's risk assessment and analyzed independently by the Safety

Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the safety evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of the overall risk assessment to the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the DMEPA staff's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the DMEPA staff provides a detailed explanation of these differences.

6. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names 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

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

the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's

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

Appendix B: FDA Prescription Study Responses (conducted March 3, 2010).

Written Outpatient	Written Inpatient	Verbal Prescription
Adasuve	Adasurc	Attisu
Adasuve	Idesuric	Adifu
Adasive	Adasuir	Adisude
Adasive	Adasuve	Atafue
Adasuve	Adasuir	Atafu
Adasucv	Adasuor	Ativan
Adasive	Adasuve	Antavu
Adasuive	Adasuvi	Adasuz
Adasuc	Idasurr	Adasuv
Adaserve	Adasuve	
Adasive		
Adarive		
Adasvic		
Adasucv		

Appendix C: Names Lacking Orthographic and/or Phonetic Similarity.

Name	Similarity to Adasuve
Adapin	Look
Adefovir (b) (4)	Look
Adoxa (b) (4)	Look
Advil (b) (4)	Sound
Alavert (b) (4)	Look
Aldomet (b) (4)	Look
Altanax (b) (4)	Look

Alteplase ((b) (4))	Look
Amidate	Look
Atorvastatin ((b) (4))	Look
Avastin ((b) (4))	Look

Appendix D: Products that have withdrawn NDA applications prior to Approval

Proprietary Name	Similarity to Adasuve	Withdrawn
(b) (4)	Look	(b) (4)
(b) (4)	Look	(b) (4)

Appendix E: Product with no product information available

Proprietary Name	Similarity to Adasuve	Commonly used references with no information found
Adocaine	Look	Drugs@FDA, Facts and Comparison, Orange Book, RedBook

Appendix F: Discontinued products with no generic equivalent products available

Proprietary Name	Similarity to Adasuve	Source
Adagin (Natural medicine)	Look	Natural Medicines Comprehensive Database

Appendix G: Products with no overlap in strength or dose.

Product name with potential for confusion	Similarity to Adasuve	Dosage Form/ Strength	Usual Recommended Dose
Adasuve (Loxapine)	N/A	Inhalation Powder: 5 mg, 10 mg	10 mg (or 1 inhalation) once (5 mg when clinically warranted)
Cida-stat (Chlorhexidine Gluconate) <i>Over-the-counter</i>	Look	Topical solution: 2%	Information not available for Cida-stat. Similar Chlorhexidine products: Wash skin with the surgical scrub solution.

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

Appendix H: Products with numerical similar strength or achievable dose with differentiating product characteristics

Product name with potential for confusion	Similarity to Adasuve	Strength	Usual Dose (if applicable)	Product Characteristics and Orthographic Differences
Adasuve (Loxapine)	N/A	Inhalation Powder: 5 mg, 10 mg	10 mg (or 1 inhalation) once (5 mg when clinically warranted)	
Adacel (vaccine for diphtheria, tetanus toxoids and acellular pertussis)	Look	Injectable: single dose vials	Single dose (0.5 mL) intramuscularly	Dosage form (injectable vs. inhalation powder), route of administration (intramuscular vs. inhalation), strength (no strength vs. 5 mg or 10 mg) Orthographics: different ending letters 'cel' vs. 'suve'; upstroke in Adacel
Atacand (Candesartan Cilexetil)	Look	Tablet: 4 mg, 8 mg, 16 mg, 32 mg	Individualized dosing; Ranges from 2 mg to 32 mg once daily orally	Dosage form (tablet vs. inhalation powder), frequency of administration (once daily vs. once), strength (4 mg, 8 mg, 16 mg, 32 mg vs. 5 mg, 10 mg) Orthographics: different ending 'cand' vs. 'suve'; upstroke 'd' in Atacand
Adcirca (Tadalafil)	Look and Sound	Tablet: 20 mg	40 mg once daily orally	Dosage form (tablet vs. inhalation powder), frequency of administration (once daily vs. once), strength (20 mg vs. 5 mg, 10 mg) Orthographics: different letters 'circa' vs. 'suve'
Aclovate (Aclometasone Dipropionate)	Look	Cream: 0.05% Ointment: 0.05%	Apply to affected area twice or three times daily	Dosage form (cream/ointment vs. inhalation powder), route of administration (topical vs. inhalation), frequency of administration (twice or three times daily vs. once) Orthographics: different letters 'vate' vs. 'suve'; upstroke 't' in Aclovate

Adagen (Pegademase Bovine)	Look	Injectable: 250 units/mL	Injection should be administered every 7 days as an intramuscular injection. Individualized dosing. 1 st dose: 10 units/kg 2 nd dose: 15units/kg 3 rd dose: 20 units/kg Maintenance dose: 20 units/kg per week.	Dosage form (injectable vs. inhalation powder), route of administration (intramuscular vs. inhalation), frequency of administration (every 7 days vs. once), dosage unit (units vs. mg) Orthographics: different letters 'gen' vs. 'suve'; downstroke of 'g' in Adagen
Adalat Adalat CC (Nifedipine)	Look	Adalat: (discontinued but generics available) Capsule: 10 mg, 20 mg Adalat CC tablet: 30 mg, 60 mg, 90 mg	Adalat: 10 mg to 20 mg three times daily Adalat CC: 30 mg to 60 mg once daily	Dosage form (tablet/capsule vs. inhalation powder), frequency of administration (once daily or three times daily vs. once) Orthographics: different letters 'lat' vs. 'suve'; difference of 2 upstrokes ('l' and 't') in Adalat
Adderall (Amphetamine)	Look and Sound	Tablet: 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, 30 mg XR capsule: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg	Individualized; Ranges from 5 mg to 30 mg once or twice daily	Dosage form (tablet/capsule vs. inhalation powder), frequency of administration (once or twice daily vs. once) Orthographics: different letters 'derall' vs. 'suve'; difference of 3 upstrokes ('d', 'l' and 'l') in Adderall
Adenocard (Adenosine)	Look	Injectable: 6 mg/2 mL (3 mg/mL) 12 mg/4 mL (3 mg/mL)	Adult: 6 mg or 12 mg via rapid intravenous bolus Children: 0.05 to 0.1 mg/kg as a rapid IV bolus	Dosage form (injectable vs. inhalation powder), route of administration (intravenous vs. inhalation), strength (3 mg/mL vs. 5 mg or 10 mg) Orthographics: different letters 'nocard' vs. 'suve'; upstroke of ending 'd' in Adenocard; Adenocard is longer (9 letters vs. 7 letters)

Adenoscan (Adenosine)	Look	Injectable: 60 mg/20 mL (3 mg/mL) 90 mg/30 mL (3 mg/mL)	140 mcg/kg/min infused for six minutes	Dosage form (injectable vs. inhalation powder), route of administration (intravenous vs. inhalation), strength (3 mg/mL vs. 5 mg or 10 mg), usage setting (diagnostic vs. treatment) Orthographics: different letters 'noscan' vs. 'suve'; Adenoscan is longer (9 letters vs. 7 letters)
Adreview (Iobenguane Sulfate I 123)	Look	Injectable: 10 mci/5 mL	Use as directed	Dosage form (injectable vs. inhalation powder), route of administration (injection vs. inhalation) Orthographics: different letters 'review' vs. 'asuve'
Antabuse (Disulfiram)	Look and Sound	Tablet: 250 mg, 500 mg	125 mg to 500 mg once daily	Dosage form (tablet vs. inhalation powder), frequency of administration (once daily vs. once) Orthographics: different letters 'ntabuse' vs. 'dasuve'; cross- stroke 't' in Antabuse vs. none in Adasuve; additional upstroke 'b' in Antabuse
Atarax (Hydroxyzine Hydrochloride) <i>*Discontinued but generics available</i>	Look	Tablet: 10 mg, 25 mg, 50 mg, 100 mg Oral syrup: 10 mg/5 mL Generics also available in injectable: 25 mg/mL, 50 mg/mL	25 mg to 100 mg three to four times daily orally or intramuscularly	Dosage form (tablet/oral syrup/injectable vs. inhalation powder), frequency of administration (three to four times daily vs. once) Orthographics: different letters 'tarax' vs. 'dasuve'; cross-stroke 't' in Atarax vs. none in Adasuve
Ativan (Lorazepam)	Look and Sound	Tablet: 0.5 mg, 1 mg, 2 mg Injectable: 2 mg/mL, 4 mg/ mL	Individualized. Oral dosing ranges from 1 mg to 6 mg in divided dose Injectable: 0.05 mg/kg intramuscularly or 0.044 mg/kg intravenously	Dosage form (tablet or injectable vs. inhalation powder) Orthographics: different letters 'tivan' vs. 'dasuve'; cross-stroke 't' in Ativan vs. none in Adasuve

Atropine	Look	Injectable: 0.05 mg/mL, 0.1 mg/mL, 0.3 mg/mL, 0.4 mg/mL, 0.5 mg/mL, 0.8 mg/mL, 1 mg/mL Ophthalmic ointment or solution: 1%	Injectable: 0.4 mg to 0.6 mg every 6 hours as needed Ophthalmic solution: 1 to 2 drops three times daily into eye Ophthalmic ointment: use once or twice daily	Dosage form (injectable or ointment/solution vs. inhalation powder), route of administration (injectable or intraocular vs. oral inhalation), frequency of administration (once to three times daily vs. once) Orthographics: different letters 'tropine' vs. 'dasuve'; cross- stroke 't' in Atropine; downstroke 'p' in Atropine
Pediasure (Over-the-counter)	Look	Oral liquid: Supplemental nutritional formula	Use as directed	Dosage form (oral liquid vs. inhalation powder), availability (over-the-counter vs. prescription) Orthographics: different beginning letter 'P' vs. 'A'; different middle letters 'edia' vs. 'da'; Pediasure is longer (9 letters) vs. Adasuve (7 letters)

Appendix I: Potential confusing name with overlap in prescribing directions

Adasuve (Loxapine)	Dosage form: Strength: Inhalation Powder: 5 mg, 10 mg	Dose: 10 mg (or 1 inhalation) once (5 mg when clinically warranted)
Failure Mode: Name confusion	Causes	Effects
Advair (Fluticasone Propionate/ Salmeterol) Diskus: 100 mcg/50 mcg, 250 mcg/50 mcg, 500 mcg/50 mcg HFA: 5 mcg/21 mcg, 115 mcg/21 mcg, 230 mcg, 21 mcg <u>Dose:</u> Diskus: 1 inhalation twice daily	Orthographic similarities: same beginning letters 'Ad'; 'v' and 's' can look similar; 'r' and 'e' can look similar Overlapping dosage form (inhalation powder) and route of administration (oral inhalation); numerical similar strength (100 mcg vs. 10 mg); overlapping dose (1 inhalation);	The orthographic and product differences minimize the likelihood of medication errors in usual practice settings. <i>Rationale:</i> Although there are orthographic and product similarities between Advair and Adasuve, the difference in frequency of administration (twice daily vs. once) in addition to difference in the dose (100 mcg/50 mcg vs. 5 mg and 10 mg) and strength unit (mcg vs. mg) may help differentiate the products. Since Advair is a combination product, the strength for both ingredients will likely be indicated on prescriptions. Additionally, the difference in dispensing setting may help to distinguish the products since Adasuve will be given as a "Stat" medication in an inpatient setting while Advair will be used as a maintenance medicine

<p>HFA: 2 inhalations twice daily</p>		<p>mostly in the outpatient setting.</p>
<p>Adenosine</p> <p>Injectable: 3 mg/mL</p> <p><i>Treatment:</i> Adult: 6 mg or 12 mg via rapid intravenous bolus</p> <p>Children (<50 kg): 0.05 to 0.1 mg/kg as a rapid IV bolus</p> <p><i>Diagnostic:</i> 140 mcg/kg/min infused for six minutes</p>	<p>Orthographic similarity: Both names start with 'Ad-'; the next letter 'e' and 'a' can look similar; remaining letters do not have upstroke, downstroke or cross-strokes to differentiate these letters</p> <p>Product characteristic similarity: achievable dose (5 mg or 10 mg); overlapping frequency of administration (once)</p>	<p>The product characteristic differences minimize the likelihood of medication errors in usual practice settings.</p> <p><i>Rationale:</i></p> <p>Although Adenosine and Adasuve look similar orthographically, the differences in product characteristics such as dosage form (injectable vs. inhalation powder), route of administration (intravenous vs. inhalation), strength (3 mg/mL vs. 5 mg or 10 mg), and dose (6 mg or 12 mg vs. 5 mg or 10 mg) minimize the risk of confusion between the name pair.</p> <p>Additionally, since Adenosine is given in acute situation, the medicine will likely be kept in a code cart and the orders are likely to be written after the medication has been administered to be added to the patient's chart.</p>

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22549	ORIG-1	ALEXZA PHARMACEUTICA LS INC	Staccato (loxapine) for Oral Inhalation

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/s/

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