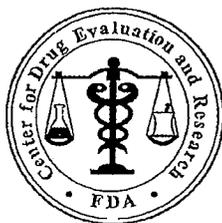


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-331

PROPRIETARY NAME REVIEW(S)



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

Date: August 13, 2009

To: Norman Stockbridge, MD, Director
Division of Cardiovascular and Renal Products

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

From: L. Shenee' Toombs, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Jenloga (Clonidine Hydrochloride) Extended-release Tablets
0.1 mg

Application Type/Number: NDA 22-331

Applicant/Applicant: Addrenex Pharmaceuticals, Inc.

OSE RCM #: 2009-1065

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

CONTENTS

EXECUTIVE SUMMARY	3
1 BACKGROUND	3
1.1 Introduction.....	3
1.2 Regulatory History.....	3
1.3 Product Information	3
2 METHODS AND MATERIALS.....	3
2.1 Search Criteria.....	4
2.2 FDA Prescription Analysis Studies.....	4
2.3 External Proprietary Name Risk Assessment	5
3 RESULTS.....	5
3.1 Database and Information Sources.....	5
3.2 Expert Panel Discussion.....	6
3.3 FDA Prescription Analysis Studies.....	6
3.4 External Study.....	6
3.5 Comments from the Division of Cardiovascular and Renal Products (DCRP)	6
3.6 Safety Evaluator Risk Assessment.....	6
4 DISCUSSION.....	7
5 CONCLUSIONS and RECOMMENDATIONS	7
5.1 Comments To The Applicant.....	7
APPENDICES	9

EXECUTIVE SUMMARY

Jenloga is the proposed proprietary name for Clonidine Hydrochloride Extended-release tablets. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name Jenloga acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Addrenex Pharmaceuticals on May 21, 2009, for an assessment of the proposed proprietary name, Jenloga, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The Applicant submitted an external study conducted by _____ in support of their proposed proprietary name. Addrenex Pharmaceuticals also submitted container labels and carton labeling for review, which will be reviewed under separate cover (OSE Review #2009-1066).

b(4)

1.2 REGULATORY HISTORY

Jenloga (Clonidine Hydrochloride) is currently under review by the Division of Cardiovascular and Renal Products under NDA 22-331 with a PDUFA goal date of September 30, 2009. Jenloga was initially reviewed under the proprietary name CloniBID (OSE Review #2008-487). DMEPA objected because the proposed name contained the dosing frequency, "BID" in addition to the initial titration period including once a day dosing. The Applicant then submitted an alternate name Sympres, which was found acceptable by DMEPA (OSE Review# 2008-853) but this proposed proprietary name was subsequently withdrawn by the applicant and the name Jenloga submitted.

1.3 PRODUCT INFORMATION

Jenloga (Clonidine Hydrochloride) is a centrally acting alpha-agonist drug being investigated for the treatment of hypertension. The recommended starting dose is 0.1 mg at bedtime. The dose may be increased by 0.1 mg at weekly intervals up to 0.6 mg daily in divided doses (i.e., morning and bedtime). Jenloga will be supplied as 0.1 mg extended-release tablets in bottles of 60 or 180 tablets.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Jenloga.

2.1 SEARCH CRITERIA

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

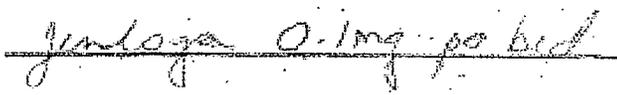
To identify drug names that may look similar to Jenloga, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (7 letters), upstrokes (two, capital letter 'J' and lowercase letter 'l'), down strokes (one, lower case letter 'g'), cross strokes (none), and dotted letters (none). Additionally, several letters in Jenloga may be vulnerable to ambiguity when scripted, including the capital letter 'J' may appear as capital letters 'L', 'F', 'H', 'G', or 'T'; lower case 'e' may look like lower case 'a', 'o' or 'c'; lower case 'n' may look like lower case 'u', 'x', 'r', 'h', 'm' or 's'; lower case letter 'l' may appear as lower case 'b', 'e', or 'f'; lower case 'o' may appear as lower case 'a', 'e', or 'c'; lower case 'g' may appear as lower case 'j', 'p', 'q' or 'y'; lower case 'a' may look like lower case 'e', 'o', or 'c'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Jenloga.

When searching to identify potential names that may sound similar to Jenloga, the DMEPA staff search for names with similar number of syllables (3), stresses (JEN-lo-ga; jen-LO-ga; jen-lo-GA), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'Jen-' may sound like 'Gen', 'Gin', and 'Jin'. The Applicant's intended pronunciation (jen-LO-gah) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 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 medication order and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Jenloga Study (conducted on June 12, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p>Inpatient Medication Order:</p> 	<p>Jenloga 0.1 mg Dispense: #60 Take 1 po qday</p>

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

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

<p><u>Outpatient Medication Order:</u></p> <p>Jenloga 0.1mg # 30 1 tab po bid</p>	
---	--

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis 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 associated with the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of twenty two names as having some similarity to the name Jenloga.

Twenty of the twenty two names (Fentora, Foligan, Gantanol, Genlip, — Genora, Gentex, Geslutin, Halog, Halog-E, Jantoven, Januvia, Jestril, Jolessa, Jolissa, —, Kenalog, Lendacin, Lentaron and Taclonex) were thought to look like Jenloga. The remaining two names (Jojoba and —***), were thought to look and sound similar to Jenloga.

b(4)

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 9, 2009.

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

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 Jenloga.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of twenty-four practitioners responded in the prescription analysis studies. Thirteen of the participants interpreted the name correctly as "Jenloga," with correct interpretation occurring in both the inpatient and outpatient written studies. The remainder of the written responses misinterpreted the drug name. The majority of misinterpretations occurred with the initial capital letter 'J' being misinterpreted as 'F', 'Z', 'I' and 'Y'. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Jenloga. The majority of misinterpretations occurred with the initial letters 'Je' being misinterpreted as 'Gi'. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

In the proposed name risk assessment submitted by the Applicant, _____ identified and evaluated a total of thirteen names thought to have some potential for confusion with the name Jenloga: Januvia, Humalog, Kenalog, Singulair, Tenormin, Desogen, Jantoven, Janumet, Jolessa, Lovaza, Methyl dopa, Novolog and Reglan. Four of the 13 names (Januvia, Kenalog, Jantoven, Jolessa) were previously identified in DMEPA staff searches. The remaining nine names were evaluated in Section 3.6 below.

b(4)

3.5 COMMENTS FROM THE DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS (DCRP)

In response to the OSE, June 10, 2009 e-mail, DCRP did not forward any comments and/or concerns on the proposed name at the initial phase of the name review.

On July 28, 2009, DMEPA notified the Division of Cardiovascular and Renal Products via e-mail that we had no objections to the proposed proprietary name, Jenloga. Per e-mail correspondence from the Division of Cardiovascular and Renal Products on August 4, 2009, they indicated that they concur with our assessment of the proposed proprietary name, Jenloga.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified four additional names (Fontego, Tenlap, _____, Zolínza) which were thought to look similar to Jenloga and represent a potential source of drug name confusion.

b(4)

Upon further observation, the name Jolissa, was found to be a misspelling of the proprietary name Jolessa. Therefore, Jolissa was eliminated from further analysis.

Thus, we evaluated a total of thirty four names for their similarity to the proposed name.

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

4 DISCUSSION

Neither DDMAC nor the Division of Cardiovascular and Renal Products had concerns with the proposed name Jenloga.

A total of thirty four names were identified and evaluated by DMEPA. Twenty three of the thirty four names lacked convincing orthographic and/or phonetic similarity to the proposed proprietary name Jenloga and were not evaluated further. (see Appendix C).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining eleven names and lead to medication errors. This analysis determined that the name similarity between Jenloga was unlikely to result in medication errors with any of the eleven products for the reasons presented in Appendices D through I. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Jenloga, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Jenloga, for this product at this time. Our assessment supports the findings of the External Study submitted by the Applicant. Additionally, DDMAC does not object to the proposed name, Jenloga, from a promotional perspective.

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 application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sean Bradley, OSE project manager, at 301-796-1332.

5.1 COMMENTS TO THE APPLICANT

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

Jenloga 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.

REFERENCES

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

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

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

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

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

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

4. *AMF Decision Support System [DSS]*

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

12. *Stat!Ref (www.statref.com)*

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

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

USAN Stems List contains all the recognized USAN stems.

14. *Red Book Pharmacy's Fundamental Reference*

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

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

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

16. *Medical Abbreviations Book*

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

APPENDICES

Appendix A:

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

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

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

³ National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/about/MedErrors.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 Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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 or Generic drugs

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

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. (See Section 4 for limitations of the process).

Appendix B: FDA Prescription Study Responses.

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Jenloga	Jenloga	Ginloga
Jenloga	Jenloga	Giloga
Fenloga	Jenloga	Jeloga
Jendoga	Jenloga	
Jenloga	Jenloga	
Jenloga	Ienloga	
Jinloga	Jenloga	
Jenloga	Jenloga	
Yenloga		
Jenloga		
Zenloga		
Jenloga		
Jinloga		

Appendix C: Proprietary names that lack convincing orthographic and/or phonetic similarities

Proprietary Name	Similarity to Jenloga
Desogen	Look _____
Gantanol	Look
_____	Look
Genora	Look
Gentex	Look
Geslutin	Look
Halog	Look
Humalog	Look and Sound _____
Jantoven	Look
Janumet	Look and Sound _____
Januvia	Look
Jolessa	Look
Jojoba	Look and Sound
Kenalog	Look
Lovaza	Look _____
Lendacin	Look
Lentaron	Look
Methyldopa	Look _____
Novolog	Look and Sound _____
Reglan	Look _____
Singulair	Look _____
Taclonex	Look
Tenormin	Look _____

b(4)

b(4)

b(4)

b(4)

b(4)

b(4)

Appendix D: Proprietary names that are internationally registered

Proprietary Name	Similarity to Jenloga	Active Ingredient	Country
Foligan	Look	Allopurinol	Germany
Fontego	Look	Bumetanide	Italy
Genlip	Look	Gemfibrozil	Italy
Jestryl	Look	Carbachol	Germany/Czech Republic

Appendix E: Proposed proprietary names that were approved under a different proprietary name

Proprietary Name	Similarity to Jenloga	Reason for Discard
—	Look and Sound	Approved under the name Aplenzin
—	Look	Approved under the name Fusilev

b(4)

Appendix F: Proposed proprietary names conditionally approved under a different proprietary name.

Proprietary Name	Similarity to Jenloga	Reason for Discard
—	Look	Secondary proprietary name Primary proprietary name, Amaya, found acceptable (OSE Review 2009-938). NDA has not been approved.

b(4)

Appendix G: Discontinued products with no available generics

Proprietary Name	Active Ingredient	Similarity to Jenloga
Halog-E	Halcinonide	Look
Tenlap ¹	Acetaminophen	Look

¹Tenlap (Acetaminophen) previously marketed as 125 mg/5 mL elixir. Currently marketed Acetaminophen liquid preparations include: Children's Tylenol (160 mg/5 mL) and Infant's Tylenol (160 mg/ 1.6 mL).

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

Appendix H: Products with no numerical overlap in strength and usual dose

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Jenloga (Clonidine) Extended-release Tablets		Tablet: 0.1 mg	<u>Treatment of Hypertension:</u> 0.2 mg-0.6 mg in divided doses (morning/bedtime)
Fentora (Fentanyl Citrate)	Look	Tablets (Buccal): 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, 800 mcg	100 mcg to 800 mcg by mouth as needed for breakthrough pain

Appendix I: Single strength products with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Jenloga (Clonidine) Extended-release Tablets		Tablet: 0.1 mg	<u>Treatment of Hypertension:</u> 0.2 mg-0.6 mg in divided doses (morning/bedtime)	
Zolinza (Vorinostat)	Look	Capsule: 100 mg	Treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma who have progressive, persistent or recurrent disease on or following two systemic therapies. Take 400 mg (4 capsules) daily with food.	Frequency of Administration: Twice daily vs. Once daily Procurement: Rx Only vs. Restricted distribution For Zolinza: -Sponsor offers ACT Program which helps coordinate access to obtaining drug. -Product not routinely stocked in local pharmacies -MD's would have to contact Drug Company to request a drop shipment

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

/s/

Latoya S TOOMBS
08/13/2009

DENISE P TOYER
08/13/2009

CAROL A HOLQUIST
08/13/2009



**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: October 24, 2008

To: Norman Stockbridge, M.D.
Director, Division of Cardiovascular and Renal Products

Through: Todd Bridges, RPh, Team Leader
Denise Toyer, Pharm D, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Diane C. Smith, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name, Label and Labeling Review

Drug Name(s): Sympres
(Clonidine Hydrochloride Extended-release Tablets) 0.1 mg

Application Type/Number: NDA 22-331

Applicant: Addrenex Pharmaceuticals, Inc.

OSE RCM #: 2008-853

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

CONTENTS

EXECUTIVE SUMMARY	3
1 BACKGROUND.....	3
1.1 Introduction.....	3
1.2 Regulatory History.....	3
1.3 Product Information.....	3
2 METHODS AND MATERIALS	4
2.1 Proprietary Name Risk Assessment	4
2.2 Label and Labeling Risk Assessment	9
3 RESULTS.....	10
3.1 Proprietary Name Risk Assessment.....	10
3.2 Label and Labeling Risk Assessment	11
4 DISCUSSION	11
4.1 Proprietary Name Risk Assessment.....	11
4.2 Label and Labeling Risk Assessment	11
5 CONCLUSIONS AND RECOMMENDATIONS.....	12
5.1 Comments to the Division.....	12
5.2 Comments to the Applicant.....	12
APPENDICES	15

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Sympres, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis has no objection to the use of the proposed proprietary name, Sympres, at this time. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels are vulnerable to confusion that could lead to medication errors. The Division of Medication Error Prevention and Analysis believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Cardiovascular and Renal Products for assessment of the proposed proprietary name, Sympres, regarding potential name confusion with other proprietary or established names. Additionally, container labels and insert labeling were submitted for evaluation for their potential to contribute to medication error.

1.2 REGULATORY HISTORY

On May 10, 2008 the Applicant submitted a 505(b)(2) application that provides for an extended-release tablet of clonidine 0.1 mg. The reference listed drug is Catapres (NDA# 17-407). The Division of Medication Error Prevention and Analysis initially reviewed the proprietary name "CloniBID" and did not recommend the use of this name because it contained the dosing frequency "BID". "BID" which infers that the product is dosed "twice daily", and this drug can be administered on a once daily dosing frequency. The Division of Cardiovascular and Renal Products concurred with our recommendation. Subsequently, the Applicant submitted the name Sympres for review.

1.3 PRODUCT INFORMATION

Sympres (clonidine hydrochloride) is a centrally acting alpha-agonist indicated in the treatment of hypertension. The recommended starting dose is 0.1 mg at bedtime. The dose may be increased by 0.1 mg at weekly intervals up to 0.6 mg daily in divided doses (i.e., morning and bedtime). Sympres will be supplied as 0.1 mg extended-release tablets in bottles of 60 tablets and 180 tablets.

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the Division of Medication Error Prevention and Analysis staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and label, labeling, and/or packaging risk assessment (see 2.2 Container Label, Carton, and Insert Labeling Risk Assessment). The primary focus for both assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention and Analysis 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

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Sympres, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Sympres, the Medication Error Prevention staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). We also conduct internal CDER prescription analysis studies (see 2.1.3), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see detail 2.1.4).

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 (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.² FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention and Analysis 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 Our Division uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, the Staff consider the product characteristics associated with the proposed drug throughout the risk assessment, since 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.

² Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

³ 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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, we consider 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.⁴

2.1.1 Search Criteria

The Medication Error Staff consider 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 'S' 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.⁵⁶

To identify drug names that may look similar to Sympres, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (7 letters), upstrokes (1, capital letter 'S'), downstrokes (two, 'y' and 'p'), cross-strokes (none), and dotted letters (none). Additionally, several letters in Sympres may be vulnerable to ambiguity when scripted, including the letter 'S' may appear as 'G'; lower case 'y' appear as a lower case 'u'; lower case 'm' may appear as 'n' and 'z'; lower case 'p' may appear as 'x' or 'y'; lower case 'r' may appear as 'n'; and lower case 'e' may appear as 'a', 'i', or 'l'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Sympres.

When searching to identify potential names that may sound similar to Sympres, the Medication Error Staff search for names with similar number of syllables (2), stresses (SYM-pres or sym-PRES), and placement of vowel and consonant sounds. In addition, several letters in Sympres may be subject to interpretation when spoken, including the letters "Sym" may be interpreted as 'Sim', 'Sin', 'Sem', 'Sen', 'Cim' or 'Cin'; the letter 'y' may be interpreted as 'i' or 'e'; the letter 'm' may be interpreted as 'n' and the letters 'pres' may be misinterpreted as 'press'. As such, the staff also considers there alternate pronunciations when identifying drug names that may sound similar to Sympres. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Sympres), the established name (clonidine hydrochloride), proposed indication (hypertension), strength (0.1 mg), dose (0.1 mg at bedtime; may increase up to 0.6 mg daily in divided doses), frequency of administration (morning and bedtime), route (oral) and dosage form the product (extended-release tablet). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

⁴ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

⁵ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁶ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

Lastly, the Medication Error Staff also consider the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name, Sympres, was provided to DMEPA to conduct a search 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 Sympres using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 6. To complement the process, the Medication Error 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 Medication Error Staff review the United States Adopted Names (USAN) stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention and Analysis to gather CDER professional opinions on the safety of the product and the proprietary name, Sympres. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of Medication Errors Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

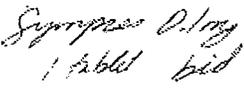
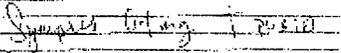
The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.3 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 Sympres 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 a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Sympres in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 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 the medication error staff.

Figure 1. Sympres Study (conducted on July 2, 2008)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u> </p>	<p>Sympres 0.1 mg 1 tablet bid</p>
<p><u>Inpatient Medication Order :</u> </p>	

2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk 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.⁷ When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention and Analysis seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike 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 a FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking: "Is the name Sympres convincing 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 Sympres 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 and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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

⁷ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Division of Medication Error Prevention and Analysis will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. We identify 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. 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 another drug product.

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

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including The Institute of Medicine, The World Health Organization, The Joint Commission, and The Institute For Safe Medication Practices, which have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the Division of Medication Error Prevention and Analysis 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Applicant, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, we believe that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If we object to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. Our Division is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for review by our Division. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container labels and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.⁸

Because Medication Error Prevention staff analyze reported misuse of drugs, we are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. We use FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product, the Applicant submitted on February 14, 2008 the following labels for our review (see Appendix K for images):

- Sample Container Label: 8 tablet count
- Retail Container: 60 and 180 tablet count
- Insert Labeling (no image)

⁸ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

Please note that the labels and labeling that the Applicant submitted contains their initial proposed proprietary name, CloniBID, which was found unacceptable by DMEPA with the review division's concurrence. We were informed by the review division that the Applicant plans to use the same labels, substituting Sympres as the proprietary name.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

In total, 21 names were identified as having some similarity to the name Sympres. Nine of 21 were thought to look like Sympres, which include: Baypress, Syntest, Symax SR, Syn-Rx, Symlin, Synarel, Simeped, Sympak [product line], and ———. Four names (Saphris***, ——— **, ——— *** and Trimplex) were thought to sound similar to Sympres. The remaining eight names (Symplex F, Symplex M, Semprex-D, ———, Enpress-28, Semprex, Symbyax and Sympt-x) were thought to look and sound similar to Sympres.

b(4)

As of July 8 2008, the proposed name, Sympres, did not contain a United States Adopted Name (USAN) stem.

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by Medication Error Staff (see section 3.1.1. above), and no additional names were thought to have orthographic or phonetic similarity to Sympres.

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

3.1.3 FDA Prescription Analysis Studies

A total of 32 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 56% of the participants (n=18) interpreted the name correctly as "Sympres", with correct interpretation occurring more frequently in the outpatient written study. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the phonetic prescription study, with the first vowel in Sympres reported as 'i' instead of 'y' or 'e' instead of 'y' and the last syllable 'pres' misinterpreted as 'press'. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator did not identify any additional names, thought to look similar to Sympres and represent a potential source of drug name confusion. As such, a total of twenty-one names were analyzed to determine if the drug names could be confused with Sympres and if the drug name confusion would likely result in a medication error. All of the identified names were determined to have some orthographic and /or phonetic similarity to Sympres, and thus determined to present some risk of confusion.

Thus, Failure modes and effects analysis (FMEA) was then applied to determine if the proposed name, Sympres, could potentially be confused with any of the twenty-one names and lead to medication errors. This analysis determined that the name similarity between Sympres and the identified names was unlikely to result in medication errors for all of the identified products for the reasons described in Appendices C through J.

3.2 LABEL AND LABELING RISK ASSESSMENT

Upon review of the container label and insert labeling, the Division of Medication Error Prevention and Analysis notes the following:

1. The dosage form “sustained-release tablets” is used throughout the labels and labeling for this product.
2. The navy blue text font for the established name and dosage form on the blue shaded background is difficult to read.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

Our evaluation found that the proposed name, Sympres, has some similarity to other proprietary drug names, but the findings of the FMEA indicates that the proposed name is not vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, the Medication Error Prevention Staff believes that these limitations are sufficiently minimized by the use of an Expert Panel, and the CDER Prescription Studies that involved 124 CDER practitioners.

4.2 LABEL AND LABELING RISK ASSESSMENT

Our Label and Labeling Risk Assessment noted that the Applicant uses the dosage form “sustained-release tablets” throughout the labels and labeling. DMEPA contacted the assigned Office of New Drug Quality Assessment (ONDQA) Chemist to discuss the proper designation of the dosage form. On September 17, 2008, the chemist noted that ONDQA will recommend that the Applicant only use the dosage form “extended-release tablets” as the proper dosage form designation for this product.

We also noted that the text used for the established name and dosage form statement on the shaded background is difficult to read because the Applicant has chosen colors that don’t provide sufficient contrast to one another (navy blue on blue shaded background). The color needs to be revised to provide more contrast and increase the readability of this statement.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Sympres, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Sympres, for this product. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the medication error prevention staff rescinds this Risk Assessment finding, and recommends that the name 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. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

The Label and Labeling Risk Assessment found the finished dosage form of the established name is incorrect and should be revised as recommended by ONDQA to read "extended-release" tablets. We also noted the font color used for the established name is insufficient to afford a maximum contrast and increased readability of the name. These issues can be addressed prior to approval. Our recommendations follow in Section 5.2.2.

5.1 COMMENTS TO THE DIVISION

We would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Sean Bradley, OSE Project Manager, at 301-796-1332.

5.2 COMMENTS TO THE APPLICANT

5.2.1 *Proprietary Name*

DMEPA has no objections to the use of the proprietary name, Sympres, for this product at this time. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the medication error prevention staff 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.

5.2.2 *Labels and Labeling*

1. Revise the established name to read Clonidine Extended-release Tablets.
2. To improve the readability, revise the color of the font used for the text of the established name and dosage form statement to maximize the contrast between the text and the background.

6 REFERENCES

1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufacturers that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential post marketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. *Micromedex Integrated Index (<http://csi.micromedex.com>)*

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

3. *Phonetic and Orthographic Computer Analysis (POCA)*

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. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

4. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://factsandcomparisons.com>)*

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

5. *AMF Decision Support System [DSS]*

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

6. *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.

7. *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.

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

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

Provides information regarding patent and trademarks.

10. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. 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.

12. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

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

13. Stat!Ref (www.statref.com)

Contains full-text information from approximately 30 texts. 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.

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

List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

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

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

A web-based searchable version of the Drug Information Handbook.

17. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. We also compare 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. The Medication Error Staff also examine 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has led to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, the Division of Medication Error Prevention and Analysis will consider the Applicant’s intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, we also considers a variety of pronunciations that could occur in the English language.

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

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<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 Downstrokes Cross-strokes	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

		<p>Dotted letters</p> <p>Ambiguity introduced by scripting letters</p> <p>Overlapping product characteristics</p>	
Sound-alike	Phonetic similarity	<p>Identical prefix</p> <p>Identical infix</p> <p>Identical suffix</p> <p>Number of syllables</p> <p>Stresses</p> <p>Placement of vowel sounds</p> <p>Placement of consonant sounds</p> <p>Overlapping product characteristics</p>	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B:

CDER Prescription Study Responses

Outpatient Prescription	Inpatient Prescription	Phonetic Prescription
Sympies	Sympres	Simpris
Sympres	Sympres	Senpress
SYNIPRES	Sympres	Simpris
Sympres	Cinpress	Simpris
Sympres	Sympres	Sympress
Sympress	Synpres	Sympress
Sympres	Sympris	
Sympres	Sympres	
Sympres	Sympres	
Synpres		
Sympres		
Synpres		
Sympres		
Sympres		

Appendix C: Names lacking convincing look-alike and/or sound-alike similarities with Sympres

Proprietary Name	Similarity to Sympres
Baypress	Look
Syntest	Look
Symax SR	Look
Syn-RX	Look
Symlin	Look
Synarel	Look
Simeped	Look
Saphris***	Sound
Trimplex	Sound
_____	Look/Sound
Enpress-28	Look/Sound
Sympt-x	Look/Sound

b(4)

Appendix D: Product withdrawn and has no generic equivalents.

Proprietary Name	Similarity to Sympres	Withdrawn pending name
_____ ***	Sound	1999

Appendix E: IND products currently under review in the Agency.

Product	Similarity to Sympres
_____ ***	Sound
_____ .***	Look

b(4)

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

Appendix F: Natural Medicines that are no longer marketed in the US and no generic equivalents available.

Product	Similarity to Sympres
Symplex F	Look/Sound
Symplex M	Look/Sound

Appendix G: Discontinued products with no generic equivalents.

Product	Similarity to Sympres	Active Ingredient	Date discontinued
Semprex	Look/Sound	Acrivastine 0.8 mg	No information available
SymPak	Look	Chlorpheniramine 8 mg/ Methscopolamine 2.5 mg/ Phenylephrine 15 mg/Guaifenesin 600 mg	July 2008
SymPak PDX		Chlorpheniramine 12 mg/ Methscopolamine 2.5 mg/ Phenylephrine 20 mg	
SymPak PDX Chewable Tablet		Chlorpheniramine 2 mg// Methscopolamine 1.5 mg/ Phenylephrine 10 mg	

Appendix H: Product with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Sympres (Clonidine Hydrochloride)		0.1 mg	1 tablet twice daily
Symbyax (Fluoxetine/Olanzapine)	Look/Sound	12 mg/25 mg, 12 mg/50 mg, 3 mg/25 mg, 6 mg/25 mg, and 6 mg/50 mg	1 capsule once daily in the evening

Appendix I: Product with single strength but has multiple differentiating product characteristics.

Product Name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose	Other differentiating product characteristics
Sympres (Clonidine HCl Extended-release)	N/A	0.1 mg	Starting dose: 0.1 mg at bedtime. Usual dose: 0.1 mg twice daily.	N/A
Semprex-D (Acrivastine and Pseudoephedrine)	Look/Sound	8 mg/60 mg	1 tablet every 4-6 hours	The inclusion of a modifier (-D) in the proprietary name, will assist in orthographically and phonetically differentiating the products. Additionally, the inclusion of the dosing frequency will assist in differentiating the products (q 4-6 h vs. bid).

Appendix J: Product with numerically similar dose

Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p align="center">Sympres (Clonidine HCl)</p>	<p>Strength: 0.1 mg</p>	<p>Usual dose: Starting dose: 0.1 mg at bedtime. Usual dose: 0.1 mg twice daily.</p>
<p>SymPak DM 2 single blister cards containing: (Chlorpheniramine 8 mg/ Methscopolamine 2.5 mg/ Dextromethorphan 30 mg/ guaifenesin 600 mg/ phenylephrine 15 mg)</p> <p>SymPak II 2 single blister cards containing: (Chlorpheniramine 8 mg/ Methscopolamine 2.5 mg/ Dextromethorphan 30 mg/ guaifenesin 600 mg/ phenylephrine 15 mg)</p>	<p>Orthographic similarity: Both drugs begin with the same first four letters "Symp".</p> <p>Overlap in route of administration (oral), dose (1 tablet) and frequency of administration (twice daily).</p>	<p>Orthographic differences in the names and differing product characteristics minimize the likelihood of medication errors in the usual practice settings.</p> <p>Rationale: The orthographic differences stem from the inclusion of the modifiers (i.e., 'DM' and 'II') which will lengthen the names and help differentiate the products when scripted.</p>

1 Page(s) Withheld

 Trade Secret / Confidential (b4)

 ✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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

/s/

Diane Smith
10/24/2008 09:30:02 AM
CSO

Todd Bridges
10/24/2008 10:41:20 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
10/24/2008 12:00:48 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
10/24/2008 03:41:41 PM
DRUG SAFETY OFFICE REVIEWER



**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: June 20, 2008

To: Norman Stockbridge, M.D., Director
Division of Cardiovascular and Renal Products

Through: Todd Bridges, RPh, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention

From: Diane C. Smith, PharmD, Safety Evaluator
Division of Medication Error Prevention

Subject: Proprietary Name Review for CloniBID

Drug Name(s): CloniBID (Clonidine Hydrochloride Extended-release) Tablets
0.1 mg

Application Type/Number: NDA # 22-331

OSE RCM #: 2008-487

1 INTRODUCTION

This memorandum is in response to a March 14, 2008 request from your Division for a review of the proprietary name, CloniBID. In the initial steps of the proprietary name review process, the Division of Medication Error Prevention identified a safety concern with the proposed name CloniBID.

2 MATERIAL REVIEWED

The Division of Medication Error Prevention reviewed the package insert submitted on February 15, 2008, and the Medical Abbreviations Book.

3 DISCUSSION

The proposed proprietary name, CloniBID, contains the dosing frequency, "BID". Inclusion of the dosing interval "BID" infers that the proposed product is dosed "twice daily". However, according to the Applicant's proposed package insert, CloniBID can be administered once daily or twice daily, hence the inclusion of "BID" in the proposed proprietary name is misleading. Additionally, we discourage the use of proprietary names that incorporate or suggest a dosing interval (e.g., NameBID). The rationale is that drug product characteristics and/or drug release characteristics are subject to change over time with approval of new dosing intervals, thus possibly rendering the original proprietary name misleading.

4 CONCLUSIONS AND RECOMMENDATIONS

The Division of Medication Error Prevention does not recommend the use of the proposed proprietary name CloniBID, since it contains the dosing interval "BID". As per email correspondence with the Division of Cardiovascular and Renal Products on June 19, 2008, the Division concurs with our assessment. Therefore, the Division of Medication Error Prevention will not proceed with the safety review of the proposed proprietary name, CloniBID. As such, the Division of Medication Error Prevention recommends that the Applicant be notified of the decision to object to the name. We will proceed with the safety review of the alternate name for this product, Sympres.

If you have any questions or need clarifications, please contact Sean Bradley, OSE Project Manager, at (301) 796-1332.

4.1 COMMENTS TO APPLICANT

1. The Division of Medication Error Prevention objects to the name CloniBID since it contains the dosing interval "BID" and this drug can be administered on a once daily dosing frequency. Thus, the name is misleading.
2. We will proceed with our safety of your alternate proposed proprietary name, Sympres.

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

/s/

Diane Smith
6/20/2008 10:08:07 AM
CSO

Todd Bridges
6/20/2008 10:38:07 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
6/20/2008 01:36:25 PM
DRUG SAFETY OFFICE REVIEWER