CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022526Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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

Date of This Review:	April 30, 2015
Application Type and Number:	NDA 022526
Product Name and Strength:	Addyi (flibanserin) Tablets 100 mg
Product Type:	Single Ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Sprout Pharmaceuticals
Panorama #:	2015-49806
DMEPA Primary Reviewer:	Loretta Holmes, BSN, PharmD
DMEPA Team Leader:	Danielle Harris, PharmD, BCPS

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Addyi, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by [redacted] (b) (4), for this product.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Addyi, on April 10, 2013. The Division of Medication Error Prevention and Analysis (DMEPA) found the name conditionally acceptable in OSE Review #2013-861, dated July 9, 2013.

The Agency issued a Complete Response Letter (CRL) on September 27, 2013. The Applicant resubmitted the NDA on February 18, 2015 in response to the CRL. Due to the length of time since our previous review of the proposed proprietary name, Addyi, a request for re-review of the name was submitted on February 18, 2015.

1.2 PRODUCT INFORMATION

The following product information is provided in the February 18, 2015 proprietary name submission.

- Intended Pronunciation: Add-e
- Active Ingredient: Flibanserin
- Indication of Use: Treatment of hypoactive sexual desire disorder
- Route of Administration: Oral
- Dosage Form: Tablets
- Strength: 100 mg
- Dose and Frequency: 100 mg once daily at bedtime
- How Supplied: 30-count bottles, trade and professional sample
- Storage: 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F)
- Container and Closure Systems: HDPE bottle with [redacted] (b) (4) cap

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Bone, Reproductive and Urologic Products (DBRUP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Addyi, was derived from a list of potential globally acceptable names. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.4 FDA Name Simulation Studies

Ninety-one (91) practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, March 4, 2015 e-mail, the Division of Bone, Reproductive and Urologic Products (DBRUP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.6 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified by (b) (4) .

Table 1. POCA Search Results	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	10
Low similarity name pair: combined match percentage score ≤49%	5

[1]USAN stem search conducted on April 22, 2015.

[2] POCA search conducted on April 7, 2015.

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 16 names contained in Table 1 determined the 16 names will not pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Bone, Reproductive and Urologic Products (DBRUP) via e-mail on April 29, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DBRUP on April 29, 2015, they stated no additional concerns with the proposed proprietary name, Addyi.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have further questions or need clarifications, please contact Shawnetta Jackson, OSE Project Manager, at 301-796-4952.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your February 18, 2015 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page)***

   USAN Stems List contains all the recognized USAN stems.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

3. ***Drugs@FDA***

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States 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* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

4. ***RxNorm***

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

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.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. 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]

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

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@FDA, CernerRxNorm, and names in the review pipeline using a 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤49%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form, etc.) may be limited when the strength or dose overlaps. We review such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

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

   In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

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

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

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

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥50% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: o Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Addyi Study (Conducted on March 10, 2015)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Addyi 100 mg po daily	Addyi Take one tablet by mouth daily Dispense #30
Outpatient Prescription: Addyi One tablet daily #30	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

			251 People Received Study 91 People Responded	
Study Name: Addyi				
Total	**31**	**28**	**32**	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
ABBIE	0	1	0	1
ADDEE	0	2	0	2
ADDI	0	4	0	4
ADDIE	0	4	0	4
ADDY	0	5	0	5
ADDYI	31	0	31	62
ADDYR	0	0	1	1
ADEE	0	1	0	1
ADI	0	8	0	8
ADIE	0	2	0	2
ADY	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed Name:** **Addyi** **Established Name:** **Flibanserin** **Dosage Form:** **Tablets** **Strength:** **100 mg** **Usual Dose:** **100 mg (1 tablet) orally once daily at bedtime**	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Addyi	100	This name is the subject of this review

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	N/A	

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** **Established name:** **Dosage form:** **Strength(s):** **Usual Dose:**	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Apri	58	The prefixes/infixes/suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different.
2.	Advil	54	The infixes/suffixes of this name pair have sufficient orthographic differences. The second syllable of this name pair sounds different.
3.	Ambi	52	The prefixes/infixes/suffixes of the name Addyi and the root name Ambi have sufficient orthographic differences. The first syllables of the name Addyi and the root name Ambi sound different.
4.	Ambi 1000/5	52	
5.	Ambi 1200	52	
6.	Ambi 40/1000/60	52	
7.	Ambi 5/15/100	52	
8.	Ambi-1000	52	
9.	Animi-3	52	The prefixes/infixes/suffixes of the name Addyi and the root name Animi have sufficient orthographic differences. The first syllable of the name Addyi and the root name Animi sound different. The root name Animi contains an extra syllable.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	Advair	42
2.	Adderall	38
3.	Adipex	34
4.	Adalat	32
5.	Actiq	30

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	N/A		

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Radri	57

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/s/

LORETTA HOLMES
04/30/2015

DANIELLE M HARRIS
04/30/2015

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

Proprietary Name Review

Date:	July 8, 2013
Reviewer(s):	Walter Fava, RPh, MSEd. Division of Medication Error Prevention and Analysis
Team Leader	James Schlick, RPh, MBA Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s):	Addyi (Flibanserin) Tablets 100 mg
Application Type/Number:	NDA 022526
Applicant/Sponsor:	Sprout Pharmaceuticals Inc.
OSE RCM #:	2013-861

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

CONTENTS

1 INTRODUCTION

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

1.1 PRODUCT INFORMATION

The following product information is provided in the April 10, 2013 proprietary name submission.

- Active Ingredient: Flibanserin
- Indication of Use: Hypoactive sexual desire in premenopausal women
- Route of Administration: Oral
- Dosage Form: Tablet
- Strength: 100 mg
- Dose and Frequency: One tablet by mouth once daily (b) (4) bedtime
- How Supplied/ Container and Closure Systems: 30 count Bottles, (b) (4)
- Storage: Controlled Room Temperature

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. The Division of Bone, Reproductive and Urologic Products (DBRUP) did not concur with OPDP's assessment. The Division expressed concerns with the name being overly promotional via e-mail on April 17, 2013. DBRUP referenced the Urban Dictionary definition of 'Yi' as 'the pinnacle of sexual excitement; the ultimate destination of pleasure; a substitute for orgasm; mainly said by Chinese people from the South' (noun), and 'to expel bodily fluids during sexual activity or when aroused' (verb). DMEPA conveyed this concern to OPDP on May 1, 2013, but OPDP maintained their non-objection to the proposed trade name, Addyi. DMEPA communicated the following rationale to DBRUP via e-mail on May 26, 2013:

- Since the product is indicated to treat sexual dysfunction in women and the intended outcome when taken is increased sexual desire and excitement, the name is not overly promotional since the intended effect of the drug is to promote sexual desire.

- The Urban Dictionary also contains 7 other slang definitions for the letter string ‘yi’, therefore it is less likely that practitioners and consumers will always relate the letter string ‘yi’ to a sexual connotation.
- The definition notes that ‘yi’ is used mainly in a subset population of Chinese people from southern China, therefore most practitioners and consumers will not be familiar with the sexual connotation with the letter string ‘yi’ in the name.
- The intended pronunciation for Addyi is ‘Add-e’, (proprietary name submitted April 10, 2013), and since the letter string ‘yi’ is pronounced with a long ‘e’ and not as ‘yee’, this will provide additional differentiation when pronouncing the name.

For these reasons, DMEPA concurs with OPDP and has no concern with the derivation of the name from a promotional perspective.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The May 1, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Addyi, has no intended meaning and was derived from a list of potential globally-acceptable names. This proprietary name is comprised of a single word that does not contain a modifier, route of administration, dosage form, etc.

2.2.3 FDA Name Simulation Studies

Seventy-three practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. Thirty-six practitioners interpreted the name correctly in the written studies, while none of the twenty-four practitioners who received the voice study responded correctly. The majority of misinterpretations in the voice study involved mistaking the ‘d’ in Addyi for the letter ‘b’ (n = 9), while other common misinterpretations involved the ending letters ‘yi’ being interpreted as ‘ie’ (n = 4), and ‘i’ (n=11). In the written studies, the most common misinterpretations involved the ending letters, ‘yi’ being interpreted as ‘yir’ (n=6) and ‘yr’ (n=3). We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, April 17, 2013 e-mail, the Division of Bone, Reproductive and Urologic Products (DBRUP) did not forward any comments or concerns relating to the safety of the proposed proprietary name at the initial phase of the review. Their promotional concerns are explained in Section 2.1 above.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Addyi. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Addyi identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. No names were identified from the FDA Prescription Simulation. Table 1 also includes names identified by (b) (4) that required further evaluation by DMEPA.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and External Name Study)					
Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Adl	FDA	Adipex-P	FDA/ (b) (4)	Aclaro	FDA
Colcrys	FDA	Advair	FDA/ (b) (4)	Aloxi	FDA
(b) (4) ***	FDA	Akten	FDA	(b) (4) ***	FDA
Alli	FDA	Addaprin	FDA	Aclovate	FDA
Adoxa	FDA	Adagen	FDA		
Adapin	FDA	Ablene	FDA		
Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Apri	FDA				
Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Addyi	FDA	Advil	FDA/ (b) (4)	Actiq	(b) (4)
Adderall	(b) (4)	Adalat	(b) (4)		

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

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Bone, Reproductive and Urologic Products via e-mail on June 26, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Bone, Reproductive and Urologic Products on June 26, 2013, they stated they still had promotional concerns with the proposed proprietary name, Addyi (see Section 2.1). The Addyi clinical team was asked to provide additional information that could further support their concern. The clinical review team did not provide additional information. Therefore, DMEPA and OPDP maintain their position that Addyi is not promotional.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Marcus Cato, OSE project manager, at 301-796-3903.

3.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The results are subject to change. If any of the proposed product characteristics as stated in your April 10, 2013 submission are altered, the name must be resubmitted for review.

4 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

   USPTO provides information regarding patent and trademarks.

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

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

9. ***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.

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

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

11. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

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

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

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

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

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

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

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

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

16. ***Walgreens (www.walgreens.com)***

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

17. ***Rx List (www.rxlist.com)***

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

18. Dogpile (www.dogpile.com)

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

19. Natural Standard (http://www.naturalstandard.com)

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

APPENDICES

Appendix A

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

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

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

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

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

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

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

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

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

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

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

1. Database and Information Sources

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

2. Expert Panel Discussion

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

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

3. FDA Prescription Simulation Studies

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

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

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

4. Comments from Other Review Disciplines

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

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

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

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

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

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

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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

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

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

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

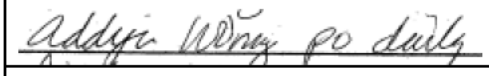
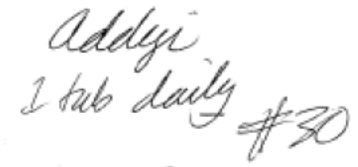
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval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

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Addyi	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Capital 'A'	Ci, Cl, G, O, t, U, H	A, E, I, O, U
Lowercase 'a'	o, u, c, e, er, ir, el, ei, ci, cl, d	ha, e, i, o, u
Lowercase 'd'	cl, ol, ci, oi	b, t
Lowercase 'y'	ef, g, j, p, q, x, v,	ee, eye
Lowercase 'i'	l	eye, ah
Letter Strings		
Ad	Acl, Ucl, Ocl, Ud, Od,	
dyi	clye, olyi, olye	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Addyi Study (Conducted on April 25, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: 	Addyi Take one tablet by mouth daily #30
Outpatient Prescription: 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

		191 People Received Study 73 People Responded
Study Name: Addyi		
OUTPATIENT	**VOICE**	**INPATIENT**
ADDEJI (1)	ABBI (1)	ADDIJA (1)
ADDYI (19)	ABBIE (1)	ADDIYR (1)
ADDYR (1)	ABBY (4)	ADDVY (1)
	ABI (3)	ADDYI (17)
	ADDI (4)	ADDYIR (6)
	ADDIE (3)	ADDYIV (1)
	ADDY (4)	ADDYR (1)
	ADEE (1)	
	ADI (3)	

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

No.	Proprietary Name	Active Ingredient	Similarity to Addyi	Failure preventions
1.	Adl		Look	No information found in any major drug reference. Name identified in Red Book Online with no product information.
2.	(b) (4)			
				Kadcyla, was approved for this product under BLA 125427
3.	(b) (4)			
				Tecfidera, was approved for this product under NDA 204063
4.	Addyi	Flibanserin	Look and Sound	Name that is the subject of this review.

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

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **Strength: 100 mg** **Usual dose:** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
5.	**Advil** (Ibuprofen) **Dosage form and strength:** Oral tablets, caplets, Liqui-Gel, and Liqui-Gel Packets: 200 mg **Usual dose:** *Rheumatoid Arthritis (RA), Juvenil RA, Juvenil Idiopathic RA, Osteoarthritis, Ankylosing Spondylitis, Acute Gouty Arthritis, Psoriatic Arthritis:* 400 mg to 800 mg three to four times a day *Dysmenorrhea, Minor aches and pains due to common cold, toothache, muscular aches, backaches:* 400 mg every 4 to 6 hours as needed *Fever* 200 mg to 400 mg every 4 to 6 hours	**Orthographic similarity:** Both names contain 5 letters and are similar in length when scripted. In addition, both names begin with the letters, 'Ad' and share the letter, 'i'. **Phonetic similarity:** Both names contain two syllables and have identical sounding first syllables ('Add' vs. 'Ad'). **Dosage form and route of administration:** Both products are available as oral tablets. **Achievable dose:** Addyi will be available as 100 mg tablets which would provide for an achievable dose of Advil 200 mg (2 x 100 mg), 400 mg (4 x 100 mg)	**Orthographic difference:** Addyi contains a second letter, 'd' and a downstroke letter, 'y', which Advil does not have. **Phonetic difference:** The second syllable, 'yi' in Addyi sounds different than the second syllable, 'vil' in Advil when spoken. **Frequency of Administration:** Once a day vs three to four times a day or every 4 to 6 hours

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **<u>Strength:</u> 100 mg** **<u>Usual dose:</u>** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
6.	**Aclaro** (Hydroquinone) **Dosage form and strength:** 4% Topical Emulsion **Usual dose:** *<u>Lentigines (freckles):</u>* Apply to affected areas twice a day *<u>Ultraviolet induced dyschromia:</u>* Apply to the affected area twice a day (morning and at bedtime)	**Orthographic similarity:** Both names begin with the letter, 'A', and the letter string, 'cl' in Aclaro may look similar to the letter, 'd' in Addyi.	**Orthographic difference:** Addyi contains the downstroke letter, 'y' which Aclaro does not have. In addition, Addyi contains three upstroke letters, 'A', 'd', and 'd', giving it a different shape when scripted compared to the two upstroke letters, 'A' and 'l' in Aclaro. **Dosing:** 100 mg or one tablet vs. one application

No.	**Proposed name:** *Addyi* **(Flibanserin) Tablets** **<u>Strength:</u> 100 mg** **<u>Usual dose:</u>** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
7.	**Colcrys** (Colchicine) **Dosage form and strength: 0.6 mg Tablets** **Usual dose:** *<u>Prevention of gout flares:</u>* 0.6mg once to twice a day *<u>Acute gout flares:</u>* 1.2 mg at first sign of gout flare x1 dose, repeat dose no sooner than 3 days *<u>Acute gout attacks:</u>* 0.6 mg every 4 hours for the first day, then every 2 hours for 2 additional doses, followed by 1.2 mg every 12 hours for 2 additional days. *<u>Prophylaxis of gout attacks during surgery:</u>* 0.6 mg three times a day 3 days before and after surgery *<u>Familial Mediterranean Fever:</u>* 1.2 mg to 2.4 mg daily in one to two divided doses *<u>Primary biliary cirrhosis</u>*: 1.2 mg daily for 5 days *<u>Dermatitis Herpetiformis or Paget's Disease:</u>* 0.6 mg three times a day	**Orthographic similarity:** The beginning letter, 'C' in Colcrys may look similar to the beginning letter, 'A' in Addyi when scripted. In addition, both names contain the letter 'y' in similar positions. **Dosage form and route of administration:** Both are oral tablets	**Orthographic difference:** Addyi contains three upstroke letters, 'A', 'd', and 'd', giving it a different shape when scripted compared to the two upstroke letters, 'C' and 'l' in Colcrys.

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **<u>Strength:</u> 100 mg** **<u>Usual dose:</u>** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
8.	**Advair** (Fluticasone and Salmeterol) **Dosage form and strength:** Inhalation powder 100 mcg/50 mcg per actuation; 250 mcg/50 mcg per actuation; 500 mcg/50 mcg per actuation **Usual dose:** Two inhalations by mouth twice a day	**Orthographic similarity:** Both names begin with the letters, 'Ad' and share the letter, 'i'. **Route of administration:** Oral **Overlapping numerical strength:** 100 mg vs. 100 mcg/50 mcg	**Orthographic difference:** Addyi contains three upstroke letters, 'A', 'd' and 'd' giving it a different shape when scripted compared to two upstroke letters, 'A', and 'd' in Advair. In addition, Addyi contains the downstroke letter, 'y' which Advair does not have. **Dose:** Tablet vs. inhalation

No.	**Proposed name:** *Addyi* **(Flibanserin) Tablets** **Strength: 100 mg** **Usual dose:** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
9.	**Aloxi** (Palonosetron) **Dosage form and strength**: 0.075 mg/1.5 mL and 0.25 mg/5 mL Injection **Usual dose:** *Chemotherapy induced nausea and vomiting:* 0.25 mg Intravenously over 30 seconds given as a single dose prior to chemotherapy	**Orthographic similarity:** Both names contain 5 letters and are similar in length when scripted. Both names begin with the letter, 'A' and end with the letter, 'i'.	**Orthographic difference:** Addyi contains three upstroke letters, 'A', 'd', and 'd', giving it a different shape when scripted compared to Aloxi which contains two upstroke letters, 'A' and 'l'. **Strength:** Single (100 mg) vs. Multiple (0.075 mg/1.5 mL and 0.25 mg/5 mL)
10.	**Akten** (Lidocaine) **Dosage form and strength:** 3.5% Ophthalmic gel **Usual dose:** Two drops applied to ocular surface in the area of the planned procedure.	**Orthographic similarity:** Both names begin with the letter, 'A' and contain five letters making them similar in length when scripted. In addition, both names also contain three upstroke letters in the same positions, ('A', 'd', and 'd' vs. 'A', 'k', and 't'), giving them a similar shape when scripted.	**Orthographic difference:** Addyi contains the downstroke letter, 'y' which Akten does not have. In addition, Akten contains the letters, 'k' and 't', which help to differentiate it from Addyi when scripted. **Frequency:** Once a day vs. One time prior to procedure and as needed during procedure.

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **<u>Strength:</u> 100 mg** **<u>Usual dose:</u>** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
11.	**Alli** (Orlistat) **Dosage form and strength:** 60 mg Capsule **Usual dose:** 60 mg by mouth three times a day with each main meal.	**Orthographic similarity:** Both names begin with the letter, 'A' and contain three upstroke letters in the same position, ('A', 'd' and 'd' vs. 'A', 'l' and 'l'). **Dosage form: Oral solid (Tablet vs. Capsule)** **Route: Oral**	**Orthographic difference:** Addyi contains the downstroke letter, 'y' which Alli does not have. **Frequency:** Once a day vs. three times a day

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **Strength: 100 mg** **Usual dose:** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
12.	**Addaprin (Ibuprofen)** **Dosage form and strength:** 200 mg Tablets *Rheumatoid Arthritis (RA), Juvenil RA, Juvenil Idiopathic RA, Osteoarthritis, Ankylosing Spondylitis, Acute Gouty Arthritis, Psoriatic Arthritis:* 400 mg to 800 mg three to four times a day *Dysmenorrhea, Minor aches and pains due to common cold, toothache, muscular aches, backaches:* 400 mg every 4 to 6 hours as needed *Fever* 200 mg to 400 mg every 4 to 6 hours	**Orthographic similarities:** Both names begin with the letters, 'Add' and contain downstroke letter, 'y' vs. 'p'. **Dosage form and route of administration:** Oral Tablet **Achievable dose:** 200 mg (2 x 100 mg), 400 mg (4 x 100 mg)	**Orthographic differences:** Addyi contains five letters and appears shorter when scripted compared to the eight letters in Addaprin. In addition, the ending letters, 'yi' in Addyi look different than the ending letters, 'rin' in Addaprin. **Frequency of Administration:** Once a day vs. three to four times a day

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **Strength: 100 mg** **Usual dose:** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
13.	**Aclovate (Aclometasone Dipropionate)** **Dosage form and strength:** 0.05% Cream and Ointment **Usual dose:** Apply a thin film to affected area two to three times daily	**Orthographic similarities:** Both names begin with the letter, 'A' and the letter string, 'cl' in Aclovate may look similar to the letter, 'd' in Addyi when scripted.	**Orthographic differences:** Addyi contains five letters and is shorter in length when scripted compared to the eight letters in Aclovate. In addition, the three upstroke letters, 'A', 'd', and 'd' in Addyi have a different pattern compared to the three upstroke letters, 'A' 'l' and 't' in Aclovate, giving the names a different shape when scripted. **Frequency of administration:** Once a day vs. two to three times a day
14.	**Adoxa (Doxycycline)** **Dosage form and strength:** 50 mg, 75 mg and 100 mg Tablets **Dose:** One tablet by mouth twice a day	**Orthographic similarities:** Both names contain five letters making them similar in length when scripted. In addition, both names begin with the letters, 'Ad'. **Dosage form and route:** Oral Tablet	**Orthographic differences:** Addyi contains three upstroke letters, 'A', 'd', 'd', and one downstroke letter, 'y', giving it a different shape when scripted compared to two upstroke letters, 'A' and 'd' in Adoxa.

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **Strength: 100 mg** **Usual dose:** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
15.	**Adagen (Pegademase Bovine)** **Dosage form and strength:** 250 units/mL Injection **Dose:** First dose: 10 units/kg intramuscularly; Second dose: 15 units/kg intramuscularly; Third dose: 20 units/kg intramuscularly; Maintenance dose: 20 units/kg per week intramuscularly	**Orthographic similarities:** Both names begin with the letters, 'Ad' and each contains a downstroke letter, 'y' vs. 'g'.	**Orthographic differences:** Addyi contains three upstroke letters, 'A', 'd', and 'd', giving it a different shape when scripted compared to two upstroke letters, 'A' and 'd' in Adagen. **Frequency:** Once a day vs. Once a week.
16.	**Adipex-P (Phentermine)** **Dosage form and strength:** 37.5 mg Capsule **Dose:** 37.5 mg by mouth once a day	**Orthographic similarities:** Both names begin with the letters, 'Ad' and contain a downstroke letter, 'y' vs. 'p'. **Dosage form and route:** Oral capsule **Frequency of Administration:** Both are given once daily	**Orthographic differences:** Addyi contains five letters and appears shorter when scripted compared to the seven letters in Adipex-P. In addition, Addyi contains three upstroke letters, 'A', 'd' and 'd', giving it a different shape when scripted compared to Adipex-P which also has three upstroke letters, 'A' , 'd' and 'P', but has the third upstroke letter in different positions.

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **<u>Strength:</u> 100 mg** **<u>Usual dose:</u>** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
17.	**Apri (Desogestrel and Ethinyl Estradiol)** **Dosage form and strength:** 0.15 mg/0.03 mg Tablet **Dose:** One tablet by mouth once a day	**Phonetic similarities:** Both names contain two syllables, with similar sounding first syllables, 'Ah'. **Dosage form and route:** Oral tablets **Frequency of Administration:** Both are given once daily	**Phonetic differences:** Apri contains an 'r' sound which helps differentiate it from Addyi when spoken.
18.	**Adapin (Doxepin Hydrochloride)** **Dosage form and strength:** 10 mg, 25 mg, 75 mg, 100 mg Capsules **Dose:** 25 mg to 300 mg by mouth in one to three divided doses.	**Orthographic similarities:** Both names begin with the letters, 'Ad' and share the letter, 'i' in similar positions in the name. **Dosage form and route:** Oral solid (Tablet vs. Capsule) **Strength:** 100 mg **Frequency:** Once a day	**Orthographic differences:** Addyi contains three upstroke letters, 'A', 'd' and 'd', giving it a different shape when scripted compared to Adapin which has two upstroke letters, 'A' and 'd'. In addition, the lower case 'a' preceding the downstroke letter, 'p' in Adapin, helps differentiate it from Addyi when scripted.

No.	Proposed name: *Addyi* (Flibanserin) Tablets **Strength:** 100 mg **Usual dose:** Take one tablet by mouth once daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
19.	**Ablene** **Dosage form and strength:** Capsules containing: Vitamin A 10,000 IU • Vitamin C 75 mg • Vitamin D (D3) 200 IU • Vitamin E 100 IU • Vitamin B1 12.5 mg • Vitamin B2 12.5 mg • Vitamin B3 50 mg • Vitamin B6 12.5 mg • Folic Acid 400 mcg • Vitamin B12 200 mcg • Biotin 10 mcg • Vitamin B5 25 mg • Iron 25.01 mg • Iodine 65 mcg • Magnesium 2.601 mg • Zinc 20 mg • Copper 0.13 mg • Manganese 3 mg • Para-Aminobenzoic Acid 12 mg • Citrus Bioflavonoids 12.5 mg • Rutin 12.5 mg • Betaine HCl 12.5 mg • Hesperidin 2.5 mg • Huperzine A extract 0.5 mg • Choline 0.08 mg • Inositol 0.13 mg • L-Glutamine 1000 mg • Cat's Claw 200 mg • Licorice 100 mg • Olive extract 50 mg **Dose:** One capsule by mouth three times a day before each meal	**Orthographic similarities:** Both names begin with the letter, 'A' and contain three upstroke letters in the same positions, 'A', 'd', 'd', vs. 'A', 'b', and 'l'.	**Orthographic differences:** Addyi contains a downstroke letter, 'y' which Ablene does not have. **Frequency:** Once a day vs. three times a day

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **<u>Strength:</u> 100 mg** **<u>Usual dose:</u>** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
20.	**Adalat (Nifedipine)** **Dosage form and strength:** 10 mg and 20 mg Capsules **Dose:** One capsule by mouth three times a day	**Orthographic similarities:** Both names begin with the letters, 'Ad' and are similar in length when scripted (5 letters vs. 6 letters). **Phonetic similarities:** The first syllable of both names is pronounced the same, 'Ad' **Dosage form and route:** Both are oral solids (tablets vs. capsules)	**Orthographic differences:** Addyi contains three upstroke letters, 'A', 'd', 'd', at the beginning of the name and has a different shape when scripted compared to Adalat which has four upstroke letters dispersed throughout the name, 'A', 'd', 'l', 't'. In addition, Addyi has a downstroke letter, 'y' which Adalat does not have. **Phonetic differences:** Addyi contains two syllables compared to three syllables in Adalat. **Frequency:** Once a day vs. three times a day
21.	**Adderall (Dextroamphetamine Amphetamine mixture)** **Dosage form and strength:** 1.25 mg, 2.5 mg, 3.75 mg, 5 mg, 6.25 mg, 7.5 mg Tablets **Dose:** One tablet by mouth once a day.	**Orthographic similarities:** Both names begin with the letter string, 'Add'. **Phonetic similarities:** The beginning syllable of both names sound alike when spoken, 'Add' vs. 'Add'. **Dosage form and route:** Both are oral tablets **Frequency:** Once a day	**Orthographic differences:** Addyi has a downstroke letter, 'y' which Adderall does not have. In addition, Addyi contains 5 letters and appears shorter when scripted compared to the 8 letters in Adderall. Also, Addyi has three upstroke letters, 'A' 'd', and 'd', giving it a different shape compared to the five upstroke letters, 'A', 'd', d' 'l', 'l' in Adderall. **Phonetic differences:** Addyi contains two syllables compared to three syllables in Adderall.

No.	**Proposed name:** ***Addyi*** **(Flibanserin) Tablets** **<u>Strength:</u> 100 mg** **<u>Usual dose:</u>** Take one tablet by mouth once daily	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
22.	**Actiq (Fentanyl Citrate)** **Dosage form and strength:** 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, 1600 mcg Buccal Lozenges **Dose:** One lozenge buccally one to four times a day as needed for breakthrough pain (200 mcg to 6400 mcg/day)	**Orthographic Similarities:** Both names contain 5 letters and are similar in length when scripted. In addition, both names begin with the letter, 'A', both names contain the letter 'i', and both names have one downstroke letter, 'y' vs. 'q'. **Phonetic similarities:** Both names contain two syllables with similar sounding first syllables, 'Ad' vs. 'Ac'. **Dosage form:** Oral solid (Tablet vs. buccal lozenge)	**Orthographic differences:** Addyi contains three upstroke letters, 'A', 'd', 'd', and has a different shape when scripted compared to two upstroke letters, 'A' and 't' in Actiq. **Phonetic differences:** The intended pronunciation of Addyi sounds like ADDEE making it sound different from Actiq (AKTEEK).

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

/s/

WALTER L FAVA
07/08/2013

JAMES H SCHLICK
07/08/2013

CAROL A HOLQUIST
07/09/2013

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	February 12, 2010
To:	Scott Monroe, MD, Director Division of Reproductive and Urologic Products
Through:	Todd Bridges, RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Deveonne Hamilton-Stokes, RN, BSN, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Girosa (Flibanserin) Tablets 100 mg
Application Type/Number:	NDA 022526
Applicant:	Boehringer Ingelheim Pharmaceuticals, Inc.
OSE RCM #:	2009-2279

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CONTENTS

EXECUTIVE SUMMARY

Girosa is the proposed proprietary name for Flibanserin 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, Girosa, conditionally 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 Boehringer Ingelheim Pharmaceuticals, Inc., dated November 20, 2009, for an assessment of the proposed proprietary name, Girosa, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, the Applicant submitted an external evaluation of the proposed proprietary name. Container labels, carton labeling and insert labeling were also submitted, but will be reviewed under separate cover.

1.2 PRODUCT INFORMATION

Girosa (Flibanserin) is indicated for treatment of Hypoactive Sexual Desire Disorder (HSDD) in premenopausal women. The usual recommended dose is 100 mg once daily at bedtime, with a maximum daily dose of 100 mg. Girosa will be available as 100 mg tablets and supplied in bottles of 30 tablets (b) (4) .

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, Girosa.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'G' 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 Girosa, 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 (six letters), upstrokes (1, capital letter 'G'), down strokes (none), cross strokes (none), and dotted letters (one, lower

[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)

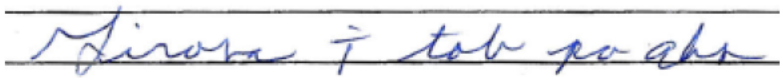
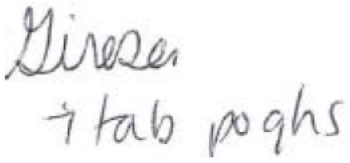
case letter 'i'). Additionally, several letters in Girosa may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Girosa.

When searching to identify potential names that may sound similar to Girosa, the DMEPA staff search for names with similar number of syllables (three), stresses (GI ro sah or gi ro SAH), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'G' may sound like 'J' and 'rosa' may sound like 'wosa'. (See Appendix B). The Applicant's intended pronunciation (gi RO sa) 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 medication order and outpatient and verbal prescriptions were communicated during the FDA prescription studies.

Figure 1. Girosa Rx Study (conducted on December 4, 2009)

HANDWRITTEN OUTPATIENT PRECRIPTIONS	VERBAL RESCRIPTION
Inpatient Order: 	Girosa take 1 tablet po qhs #30
Outpatient Prescription : 	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an independent risk assessment 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 the Division of Medication Error Prevention and Analysis staff'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 names could lead to medication errors in usual practice settings.

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

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

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

Seventeen of the names were thought to look like Girosa. They include: Alvesco, Azasan, Canasa, Ceron DM, Crinone, Crixivan, Curasore, Genesa, Genora, Geravim, Glucose, Glynase, Prozac, Samsca, Serax, Serzone, and Soma. The remaining name (b) (4) *** was thought to look and sound like Girosa.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of January 21, 2010.

3.2 CDER 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 Girosa.

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 15 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 13 % of the participants (n=2) interpreted the name correctly as "Girosa", with correct interpretation occurring in the verbal study and inpatient study. The remainder of the respondents (n=13) misinterpreted the drug name. In the inpatient medication order study respondents misinterpreted the beginning letter "G' as the letter 'L; the letter 'r' was misinterpreted as the letter 'n' and the letter 's' was misinterpreted as the letters 'v' and 'n'. In the outpatient prescription study the letter 'o' was misinterpreted as the letter 'e' and the ending letter 'a' was misinterpreted as the letter 'e' or the letters 'ei', 'er' or 'en'. In the verbal prescription study the capital letter 'G' was misinterpreted as the letter 'J' and the letter 'i' was misinterpreted as the letter 'e'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL PROPRIETARY NAME ASSESSMENT

In the proposed name risk assessment submitted by the Applicant, a total of 24 drug names were identified as having some potential for confusion with the name Girosa.

Of the 24 names, DMEPA identified the following 2 names during the database searches: Genora and Prozac/Prozac weekly. The remaining 22 names (Januvia, Jolessa, Ginkgo, Ginseng, Iressa, Mirena, Iosat, Geodon, Crotan, Proscar, Iron Dextran, Iron Sucrose, Frova, Rowasa, Thyrosafe, Gastromark, Sfrowasa, Prosol 20 % Sulfite Free in plastic container, Aerospan HFA, Iloprost, Droxia and Nitrostat) were evaluated as part of the safety evaluator risk assessment.

3.5 COMMENTS FROM THE DIVISION OF REPRODUCTIVE AND UROLOGIC PRODUCTS

3.5.1 Initial Phase of Review

The Division of Reproductive and Urologic Products (DRUP) did not respond to the December 8, 2009 e-mail sent by OSE during the initial phase of the name review inquiring about any comments and/or concerns they may have about the proposed name.

3.5.2 Midpoint Review

On January 13, 2009, DMEPA notified the Division of Reproductive and Urologic Products via e-mail that we had no objections to the proposed proprietary name, Girosa. Per e-mail correspondence from the Division of Reproductive and Urologic Products on January 13, 2009, they did not forward any comments that would find the name unacceptable based upon other factors (e.g. clinical, chemistry. DRUP indicated that they did not have any objections to the proposed proprietary name, Girosa.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

The Expert Panel identified a total of 18 names as having some similarity to Girosa. Twenty-two names were identified by the external risk assessment presented by the Applicant. Independent searches by the primary Safety Evaluator did not identify any additional names thought to look or sound similar to Girosa and represent a potential source of drug name confusion. Thus, a total of 40 names were evaluated for their similarity to the proposed name.

4 DISCUSSION

4.1 PROMOTIONAL REVIEW

DDMAC did not have promotional concerns with the proposed name, Girosa. DMEPA and DRUP concurred with DDMAC's assessment.

4.2 SAFETY REVIEW

DMEPA sought input from all stakeholders (i.e., clinical, DDMAC, CMC) on the proposed proprietary name. These stakeholders did not have concerns with the proposed name. DMEPA did not identify any aspects of the name that would function as a potential source of error other than the identification of 40 names with some similarity to the proposed name Girosa. DMEPA then evaluated these 40 names for their potential similarity to the proposed name. Twenty-one names were eliminated from further analysis due to the following reasons: Nineteen names lacked orthographic and/or phonetic similarity to Girosa, one name had no additional information in commonly used drug references; one name is no longer marketed and does not have any generics available (see Appendices D through F).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 19 names and lead to medication errors. This analysis determined that the name similarity between Girosa and these 19 products was unlikely to result in medication errors for the reasons presented in Appendices G through I. This finding was consistent with the independent risk assessment of the proprietary name submitted by the Applicant.

In addition to no look-alike or sound-alike concerns, no other factors were identified that would render the name unacceptable at this time.

5 CONCLUSIONS AND RECOMMENDATIONS

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

However, if any of the proposed product characteristics as stated in this review are altered, 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. The proposed

name must be re-reviewed 90 days before approval of the NDA. For questions or clarifications, please contact Maria Wasilik, OSE Project Manager, at 301-796-0567.

5.1 COMMENTS TO THE APPLICANT

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

Girosa will be re-reviewed 90 days prior to 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 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

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

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

proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

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

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

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

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

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the

proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of

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

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

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

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

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

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

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

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

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

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

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

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

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

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

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

Appendix B: Potential orthographic or phonetic misinterpretations of the letters in Girosa

Letters in Name, Girosa	Scripted may appear as	Spoken may be interpreted as
Capital 'G'	C, L,	J
lower case 'i'	c, e, l	any vowel
lower case 'r'	c, n, s, v	wr
lower case 'o'	a, e, u	any vowel
lower case 's'	n, r, v	c
lower case 'a'	e, u	any vowel

Appendix C:

CDER Prescription Study Responses

Inpatient Medication Order	Voice Prescription	Outpatient Prescription
Girosa	Jerosa	Girese
Linova	Girosa	Giresei
Girona		Gireser
Girova		Girese
Lirosa		Gireser
		Giresen
		Girese
		Gireser

Appendix D: Names without convincing look-alike and/or sound-alike similarities to Girosa

Proprietary Name	Similarity to Girosa
Crixivan	Look
Prozac/ Prozac Weekly	Look
Serax	Look
Januvia	External Name Study
Jolessa	External Name Study
Ginkgo	External Name Study
Proscar	External Name Study
Iron Dextran	External Name Study
Iron Sucrose	External Name Study
Frova	External Name Study
Rowasa	External Name Study
Thyrosafe	External Name Study
Gastromark	External Name Study
Sfrowasa	External Name Study
Prosol 20% Sulfite Free	External Name Study
Aerospan HFA	External Name Study
Iloprost	External Name Study
Droxia	External Name Study
Nitrostat	External Name Study

Appendix E: Drug product that is discontinued and no generic equivalent is available

Proprietary Name (Active Ingredient)	Similarity to Girosa	Status
Genesa (Arbutamine Hydrochloride)	Look	Discontinued per Orange Book and product not found in 2009 Redbook

Appendix F: Product with no additional information found in DMEPA References 1-16

Proprietary Name	Similarity to Girosa	Additional Information
Geravim Liquid	Look	Over the counter multivitamin with iron per drugs.com

Appendix G: Products available in multiple, non-overlapping product strengths

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Dosage Form/Strength	Usual Dosage Recommendations
Girosa (Filbanserin)	**NA**	**Tablets: 100 mg**	**1 tablet by mouth at bedtime**
Alvesco (Ciclesonide)	Look	Metered Aerosol: 80 mcg, 160 mcg	80 mcg, 160 mcg or 320 mcg twice daily by oral inhalation
Crinone (Progeterone)	Look	Vaginal Gel: 4 %, 8 %	Assisted Reproductive Technology: 8 % (90 mg) vaginally once or twice daily Secondary Amenorrhea: 4 % (45 mg) vaginally every other day up to a total of six doses
Glynase (Glyburide)	Look	Tablet: 1.5 mg, 3 mg, 6 mg	Starting Dose: 1.5 mg to 3 mg daily by mouth with breakfast Maintenance Dose: 0.75 mg to 12 mg daily as a single dose or in divided doses
Samsca (Tolvaptan)	Look	Tablet: 15 mg, 30 mg	Starting Dose: 15 mg once daily by mouth; Dosage may be increased at intervals greater than 24 hours to 30 mg once daily to a maximum of 60 mg once daily as need to raise serum sodium.
Soma (Carisoprodol)	Look	Tablet: 250 mg, 350 mg	250 mg to 350 mg by mouth three times a day and at bedtime
Genora 1/35 (Ethinyl Estradiol and Norethindrone) Genora 1/50 (Mestranol/norethin-drone)	Look and Sound	Tablets: 1 mg/0.35 mg, 1 mg/0.50 mg	Take 1 tablet daily
[redacted]			

(b) (4)

Appendix H: Products with single strength availability but multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Dosage form/Strength	Usual Dose (if applicable)	Other differentiating product characteristics
Girosa (Filbanserin)	**NA**	**Tablets: 100 mg**	**1tablet by mouth at bedtime**	
Canasa (Mesalamine)	Look	Rectal Suppository: 1000 mg	1 suppository in recum at bedtime for three to six weeks	Dosage form (tablet vs. suppository) Route of administration (oral vs. per rectum) Additionally, an order for Canasa may include a descriptor such as insert or may be written as "use as directed".
Mirena (Levonorgestrel)	External study	Intrauterine Device: 52 mg	Device is inserted into uterus by trained healthcare provider	Route of administration (oral vs. intrauterine) Dosage form (tablet vs.intrauterine system) Frequency of administration (once daily vs. one time for up to 5 years) Additionally, Mirena must be inserted by a trained healthcare worker using aseptic technique.
Iosat (Potassium Iodide)	External study	Tablet: 130 mg	1 tablet by mouth every 24 hours	Over the counter product to only be used as directed by Public officials in the event a nuclear radiation emergency happens
Crotan (Crotamiton)	External study	Lotion: 10 %	Massage into affected area, may repeat as needed	Route of administration (oral vs. topical) Dosage form (tablet vs. lotion) Additionally, an order for Crotan may include a descriptor such as massage, rub or may be written as "use as directed".

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Dosage form/Strength	Usual Dose (if applicable)	Other differentiating product characteristics
Girosa (Filbanserin)	**NA**	**Tablets: 100 mg**	**1tablet by mouth at bedtime**	
Curasore (Pramoxine Hydrochloride)	Look	Topical swab: 1 %	Apply to affected area as needed for fever blister	Route of administration (oral vs. topical) Dosage form (tablet vs. swab) Status (Prescription vs. Over the counter) Additionally, an order for Curasore may include a descriptor such as "apply" or may be written as "use as directed".
Ceron DM (Dextromethorphan Hydrobromide, Chlorpheniramine Maleate, Phenylephrine hydrochloride)	Look	Oral Drops: 3 mg/1 mg/3.5 mg Syrup: 4 mg/15 mg/12.5 mg per 5 mL	Drops: 0.75 mL to 1 mL four times a day depending on age Syrup: 5 mL every 4 to 6 hour	Frequency of administration (once daily vs. every 4 hours as needed) Units of measurement: (mL vs. mg) Usual dosage: (5 mL vs. 100 mg)
Ceron (Phenylephrine hydrochloride and Chlorpheniramine Maleate)		Oral Drops: 3.5 mg/1 mg Syrup: 12.5 mg/4 mg	Drops: 0.75 mL to 1 mL four times a day depending on age Syrup: 5 mL every 4 to 6 hour	
Glucose	Look	Gel: 40%	10 gram to 20 gram by mouth as needed; may repeat in 10 minutes	Dosage form (tablet vs .gel) Frequency of administration (once daily vs. one time as needed, may repeat once) Status (Prescription vs. Over the counter)

Appendix I: Potential confusing names with overlapping or achievable dose; however, risk of confusion with Girosa minimized because of other differentiating product characteristics and/or orthographic differences

Failure Mode: Name Confusion	Causes (could be multiple)	Rationale why medication errors are unlikely to occur in the usual practice setting
Girosa **(Filbanserin)** **Tablets: 100 mg**		**1 tablet by mouth at bedtime**
Azasan (Azathioprine) Tablets: 25 mg, 50 mg, 75 mg, 100 mg Renal Homotransplantation: Initial dose: 3 mg to 5 mg/kg daily beginning at time of transplant Maintenance dose: 1 mg to 3 mg/kg daily Rheumatoid Arthritis: Initial dose: 1 mg/kg by mouth given as a single dose or on a twice-daily schedule; dose increments should be at 0.5 mg/kg daily up to a maximum dose of 2.5 mg/kg/day	Orthographic similarity: Both share the same or similar letters 'osa' vs. 'asa' in similar positions; capital letter 'G' may look like capital letter 'A' when scripted Same route of administration: oral Same dosage form: tablets Overlapping strength: 100 mg Overlapping frequency of administration: daily	Although Girosa and Azasan share overlapping product characteristics, orthographic differences in the name as well as differentiating product characteristics will help reduce the risk of medication errors. The beginning of the product names help to provide orthographic differentiation 'ir' vs. 'z' help to provide orthographic distinction, as well as the ending letter 'n' in Azasan.
Serzone (Discontinued, generics available) (Nefazodone Hydrochloride) Tablet: 50 mg, 100 mg, 150 mg, 200 mg, 250 mg Starting Dose: 100 mg to 200 mg by mouth administered in two divided doses Usual Maintenance: 300 mg to 600 mg by mouth twice a day	Orthographic similarity: Both share the same or similar letters 'ir' vs. 'er' in the same positions; capital letter 'G' may look like capital letter 'S' when scripted; both share the letter 'o' in similar positions Same route of administration: oral Same dosage form: tablets Overlapping strength: 100 mg	Orthographic differences in the name as well as differentiating product characteristics will help reduce the risk of medication errors. Serzone contains a downstroke letter 'z' in the middle and when scripted appears longer than Serzone. The products have a different frequency of administration (daily at bedtime vs. twice a day). Also, because Girosa is a single strength product the strength may be omitted and thus the order could be "take 1 tablet at bedtime".

Iressa (Gefitinib) Tablet: 250 mg 1 tablet by mouth daily	<u>Orthographic similarity:</u> Both share similar letters 'rosa' vs. 'ressa' Same route of administration: oral Same dosage form: tablets Both single strength products Same frequency of administration: daily	Orthographic difference in the name will help reduce the risk of medication errors. Orthographic difference: Beginning letters 'G' vs. 'I' look distinct and the two letter 's' in Iressa help to elongate the name.
Geodon (Ziprasidone Hydrochloride) Capsule: 20 mg, 40 mg, 60 mg, 80 mg Injection: 20 mg/mL 20 mg to 100 mg by mouth twice daily 10 mg to 20 mg intramuscularly; max dose of 40 mg per day	<u>Orthographic similarity:</u> Both begin with the letter 'G'; both share the letter 'o' in similar positions Same route of administration: oral Similar dosage forms: tablet vs. capsule Achievable strength: 100 mg	Orthographic differences in the name as well as differentiating product characteristics will help reduce the risk of medication errors. Geodon contains an upstroke letter 'd' in the middle of the name and the products endings 'sa' vs. 'on' are not similar. Additionally, the products have a different frequency of administration (daily at bedtime vs. twice a day).
Ginseng 100 mg to 400 mg by mouth per day	<u>Orthographic similarity:</u> Both begin with the letters 'Gi'; both share the letter 's' in similar positions Same route of administration: oral Similar dosage forms: tablet vs. capsule Overlapping dose: 100 mg	Orthographic differences in the name as well as differentiating product characteristics will help reduce the risk of medication errors. The middle letters appear different ('ro' in Girosa and the letter 'n' in Ginseng) and the ending letters 'ng' in Ginseng provides distinction. Additionally, Girosa is a prescription product whereas Ginseng is an over the counter herbal and would not likely be written on a prescription.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22526	ORIG-1	BOEHRINGER INGELHEIM PHARMACEUTICALS INC	FLIBANSERIN

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TODD D BRIDGES on behalf of DEVEONNE G HAMILTON-STOKES
02/12/2010

DENISE P TOYER
02/12/2010

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