CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	November 16, 2010
Application Type/Number:	NDA 022574
Through:	Melina Griffis, R.Ph, Team Leader Denise Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis
From:	Anne Crandall, PharmD Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Safyral (Drospirenone, Ethinyl Estradiol, Levomefolate Calcium Tablets and Levomefolate Calcium Tablets) 3 mg/0.03 mg/0.451 mg and 0.451 mg
Applicant:	Bayer Healthcare Pharmaceuticals
OSE RCM #:	2010-1983

CONTENTS

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Safyral, is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Safyral, acceptable in OSE Review # 2010-1236 dated August 27, 2010. DDMAC reviewed the proposed name on June 10, 2010 and had no concerns regarding the proposed name from a promotional perspective. Furthermore, the review Division did not have any concerns with the proposed name, Safyral, during our initial review.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. We used the same search criteria used in OSE Review # 2010-1236 for the proposed proprietary name, Safyral. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern.

Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN update. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

The DMEPA staff did not identify any USAN stems in the proposed proprietary name, Safyral, as of November 8, 2010. However, the database searches yielded one new name (b) (4) which was thought to sound similar to Safyral and represent a potential source of drug name confusion.

3 DISCUSSION

Failure mode and effect analysis (FMEA) was applied to determine if the proposed name could potentially be confused with the name identified by DMEPA and lead to medication errors. This analysis determined that the name similarity between Safyral and the name identified was unlikely to result in medication errors for the reasons presented in Appendix A.

4 CONCLUSIONS AND RECOMMENDATIONS

The re-review determined that the proposed proprietary name, Safyral, is not vulnerable to name confusion because the proposed name (b) (4) is for a product that is still in the IND phase. The product is not currently marketed; therefore could not lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Safyral, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Reproductive and Urologic Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

5 REFERENCES

1. ***OSE reviews # 2010-1236, Proprietary Name Review Safyral, August 27, 2010, Crandall, A.***

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

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

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

USAN Stems List contains all the recognized USAN stems.

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

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

Appendix A: Drug name with differentiating product characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Differentiating Product Characteristics Safyral vs. product
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/0.03 mg /0.451 mg oral tablet 0.451 mg oral tablet**	**One tablet by mouth once daily**	
(b) (4)				

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

/s/

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11/16/2010

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Department of Health and Human Services

Food and Drug Administration

Center for Drug Evaluation and Research

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Date:	August 27, 2010
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Through:	Melina Griffis RPh, Team Leader Denise Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
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Applicant/sponsor:	Bayer Pharmaceuticals
OSE RCM #:	RCM 2010-1236

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

CONTENTS

EXECUTIVE SUMMARY

This review summarizes the proprietary name evaluation of Safyral (drospirenone/ethinyl estradiol/levomefolate calcium tablets and levomefolate calcium 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, Safyral, acceptable for this product. DMEPA considers this a final review, however , if approval of the NDA is delayed beyond 90 days from the date of this review, the proposed proprietary name, Safyral, must be re-evaluated.

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 Bayer Pharmaceuticals dated June 2, 2010 for an assessment of the proposed proprietary name, Safyral, regarding potential name confusion with other proprietary or established drug names in the usual practice setting. A previously proposed proprietary name for this product, (b) (4), was found unacceptable due to orthographic similarity with Balziva. The Applicant submitted container labels, carton and package insert labeling for this product which are currently undergoing analysis as a separate review, OSE #2010-1248.

1.2 REGULATORY HISTORY

The parent product, Yasmin, which contains drospirenone and ethinyl estradiol, was approved May 11, 2001. The proposed product, Safyral, contains the same strength of drospirenone and ethinyl estradiol as the parent product with the addition of Levomefolate calcium, which has been added to improve the folate status of women of child bearing age.

1.3 PRODUCT INFORMATION

Safyral (drospirenone,/ethinyl estradiol, levomefolate calcium tablets and levomefolate calcium tablets) is indicated for prevention of pregnancy and improvement in folate status. The recommended dose is one tablet by mouth once daily. Safyral will be supplied in a 28 day pack which will contain 21 tablets of Drospirenone, Ethinyl Estradiol and Levomefolate and seven tablets of Levomefolate.

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, Safyral.

2.1 SEARCH CRITERIA

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

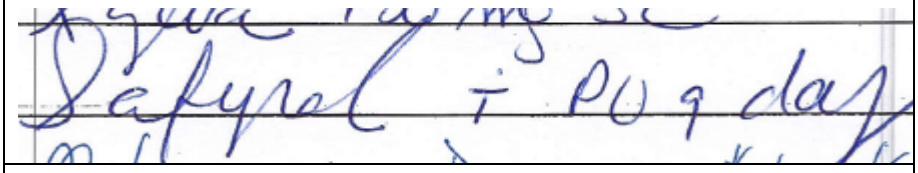
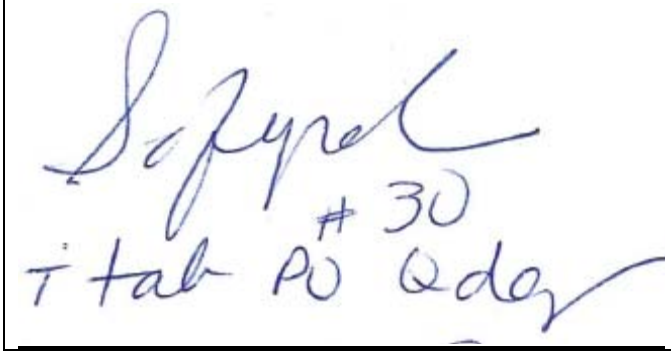
To identify drug names that may look similar to 'Safyral', the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (three, capital letter 'S' and lower case letters 'f' and 'l'), downstrokes (two, lower case 'f' and 'y'), dotted letters (none) and cross-strokes (one, 'f') . Additionally, several letters in Safyral 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 Safyral.

When searching to identify potential names that may sound similar to Safyral, the DMEPA staff searches for names with similar number of syllables (three), stresses (SA-fy-ral, sa-FY-ral, or sa-fy-RAL), and placement of vowel and consonant sounds. Pronunciation of Safyral was not provided by the Applicant. However, DMEPA staff take into consideration that pronunciation of parts of the name can vary (See Appendix B). Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Rx Study 0810 and 0813

Handwritten Medication Order	**Verbal Prescription**
	Safyral One tablet once a day
	

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)

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk associated with proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessment differs, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA safety evaluator searches yielded a total of 14 names as having some similarity to the name Safyral. Nine names (Desyrel, Saf-Gel, Saljet, Sufenta, Sulfoxyl, Sal-Plant, Salagen, Salflex, and Sudafed) were designated as orthographically similar to Safyral. One name Cefadyl was designated as phonetically similar to Safyral and the remaining four names (Sabril, Safyral, Saphris and Cefzil) were designated as both phonetically and orthographically similar.

A search of the United States Adopted Name stem list on August 2, 2010 did not identify any United States Adopted Names (USAN) stem within the proposed name, Safyral.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Safyral.

DDMAC had no concerns regarding the proposed name from a promotional perspective.

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 28 practitioners responded. None (n=0) of the respondents interpreted the name correctly as 'Safyral'. Common misinterpretations included; 'f' for 'ph', 'y' for 'a', 'o', 'i' or completely deleting the second syllable, and 'a' (in the third syllable) for 'e' 'i' or 'o'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies. One of the voice prescription study responses included a currently marketed medication, Zestril, which was also found by the primary safety evaluator. Zestril was included in the FMEA (Appendix D) for which evaluated Zestril's potential for medication error with Safyral.

3.4 EXTERNAL STUDY

In the proposed name risk assessment submitted by the Sponsor, (b) (4), found the name acceptable. (b) (4) (b) (4) found no significant look-alike or sound-alike medication names or medical terms for the proposed proprietary name. (b) (4) has devised a scale for the level of vulnerability that forecasts the probability of errors with the proposed proprietary names. This scale is based on the numbers 1-5, with 1 being the most vulnerable and 5, the least vulnerable. (b) (4) designated Safyral as a 5.

3.5 COMMENTS FROM THE DIVISION OF REPRODUCTIVE AND UROLOGY PRODUCTS (DRUP)

In response to the OSE e-mail on August 11, 2010, the Division of Reproductive and Urology Products did not forward any comments or concerns on the proposed proprietary name at the initial phase of the review.

DMEPA notified DRUP via e-mail on August 11, 2010 that we have no objections to the proposed proprietary name Safyral. Per e-mail correspondence from DRUP on August 11, 2010, they indicated they concur with our assessment of the proposed proprietary name, Safyral.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified 16 additional names that have some similarity to Safyral. Thirteen names (Sectral, Zestril, Vistaril, Sandril, Sarisol, Cafgesic, Cal-Gest, Calagel, Scytera, Selfemra, Soyacal, Sulfair, and (b) (4) ***) were designated as orthographically similar to Safyral. The remaining three names (Statrol, Synarel, and Desferal) were designated as orthographically and phonetically similar to Safyral.

Additionally, no other aspects of the name were identified as additional sources of error. Thus, a total of 30 names were identified as names with some similarity to Safyral.

4 DISCUSSION

Safyral is the proposed proprietary name for Drospirenone, Ethinyl Estradiol and Levomefolate Calcium Tablets and Levomefolate Calcium 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 review considered comments from the Division and DDMAC.

4.1 PROMOTIONAL ASSESSMENT

DDMAC did not have promotional concerns with the proposed name, Safyral. The Division of Reproductive and Urology Products and DMEPA concurred with DDMAC's assessment.

4.2 LOOK-ALIKE AND SOUND ALIKE ANALYSIS

DMEPA evaluated 30 names for their potential similarity to the proposed proprietary name Safyral. One of the 30 names was eliminated from further analysis at the initial screening because the name Safyral is the subject of this review. Therefore, 29 names were determined to have some orthographic and/or phonetic similarity to Safyral, and thus determined to present some risk for confusion.

Failure Mode and Effects Analysis (FMEA) was then applied to determine if the proposed name, Safyral, could potentially be confused with the remaining 29 names and lead to medication errors. This analysis determined that the name similarity between Safyral was unlikely to result in medication errors with any of the 29 products for the reasons presented in Appendix D.

Thus, based on DMEPA's proprietary risk assessment we determined the name was acceptable for the reasons listed above. This determination was shared with the review Division, who concurred with our assessment. Additionally, our assessment of the proposed proprietary name concurred with the conclusions of (b) (4) external name review.

5 CONCLUSIONS AND RECOMMENDATIONS

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

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, 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. Furthermore, if the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

If you have further questions or need clarifications, please contact Maria Wasilik, OSE Project Manager at 301-0567.

5.1 COMMENTS TO THE APPLICANT

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

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

If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review. The conclusions upon re-review are subject to change.

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.

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

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

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

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

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

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of 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 Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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

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

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

Type of similarity	**Considerations when searching the databases**		
	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-stokes 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. 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

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

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

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

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

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

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

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Safyral	Scripted may appear as	Spoken may be interpreted as
S	G, L, T, F, Z	“Z”, “C”
a	a, o ,e	“e”
f	t, l	
y	y, g	“i”, “a” or silent
r	v, n	
a	a, o, e	“i” or “y”
l	e	

Appendix C: FDA Prescription 0810 and 0813 Study Responses

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Safyrel	Sofyrd	Saforil
Safyrel	Sofyrel	Safaril
Safyrel	Sofyrel	Safril
Safyrel	Sofyrel	Sapharil
Safyrol	Sofyrd	Safril
Safyrel	Sofyrel	Safaril
Safyrel	Sofyrel	Safril
	Sofyrd	Safrill
		Saffro
		Safril
		Saforil
		Saphoril
		Zestril

Appendix D: Name confusion is prevented by the combination of stated product characteristics and/or orthographic differences as described

Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**	**Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described**
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Desyrel (Trazodone Hydrochloride)	Orthographic	50 mg, 150 mg, 300 mg oral tablet	Initial dose of 150 mg by mouth per day in divided doses up to 600 mg per day in divided doses	*Orthographic differences* - 'D' in Desyrel does not resemble 'S' in Safyral when scripted - Safyral has three upstrokes vs. two in Desyrel *Product characteristic differences* - Frequency of administration (once daily vs. multiple doses per day) - Strength (Single strength, most likely not written on prescription vs. various strengths 50 mg, 150 mg, 300 mg)
Sectral (Acebutolol)	Orthographic	200 mg oral capsule	200 mg to 1200 mg by mouth once or twice daily	*Orthographic differences* - Safyral has two downstrokes vs. Sectral has no downstrokes - Safyral has one letter between the first two upstrokes vs. Sectral has two letters between the first two upstrokes
Statrol (Neomycin and Polymixin B Sulfates Opthlmic Ointment, USP) (Neomycin Sulfate adn Polymixin B Sulfate Ophthalmic Solution, USP)	Orthographic and Phonetic	3.5 mg tube ophthalmic ointment 5 mL bottle	Instill about a half-inch ribbon into the conjunctival sac(s) up to three or four times daily or with the solution at bedtime Instill one or two drops in the lower conjunctival sac(s) three or more times daily as required	*Orthographic differences* - Safyral has three upstrokes vs. Statrol has four upstrokes - Safyral has one possible cross-stroke, depending on the script vs. Statrol has two cross-strokes - Safyral has one downstroke vs. Statrol has no downstrokes *Phonetic differences* - Safyral starts with the sound "saf" vs. "stah" *Product characteristic differences* - Route of administration (oral vs. eye) - Frequency of administration (once daily vs. three to four times daily)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Synarel (Nafarelin Acetate)	Orthographic and Phonetic	2 mg/mL, 8 mL bottle of nasal solution	Two sprays in each nostril in the morning and evening (8 sprays per day) or 3 sprays alternating nostril three time daily (9 sprays per day)	*Orthographic differences* - Safyral has three upstrokes vs. Synarel has two - Safyral has a downstroke in the middle of the name vs. Synarel has a downstroke as the second letter *Product characteristics* - Route of administration (oral vs. nose) - Frequency of administration (once daily vs. two to three times daily) - Dose (one tablet vs. two or three sprays)
Desferal (Desferoxamine Mesylate)	Orthographic and Phonetic	500 mg, 2 g vial of lyophilized powder	1000 mg intramuscularly once followed by 500 mg intramuscularly every 4 hours for 2 doses, can repeat 500 mg dose every 4 to 12 hours. Maximum dose in 24 hours is 6000 mg 1000 mg intravenously at a rate of 15 mg/kg/hour and then 500 mg every 4 hours for 2 doses, can repeat 500 mg dose every 4 to 12 hours. Maximum dose 6000 mg/day	*Orthographic differences* - 'S' in Safyral does not resemble 'D' in Desferal when scripted - Safyral has one or two downstrokes, depending on how 'f' is scripted vs. Desferal has no downstrokes or one depending on how 'f' is scripted Phonetic differences - The first syllable in Safyral sounds like "sahf" vs. "dess" in Desferal *Product characteristics* - Dose (1 tablet vs. 500 mg or 1000 mg) - Route of administration (oral vs. intramuscular or intravenous) - Frequency of administration (once daily vs. every 4 hours to 12 hours)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Zestril (Lisinopril)	Orthographic	2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, 40 mg oral tablet	2.5 mg to 40 mg by mouth once daily	*Orthographic differences* - 'S' in Safyral does not resemble 'Z' in Zestril when scripted - Safyral has two downstroke vs. Zestril has no downstrokes *Product characteristic differences* - Strength (single strength, most likely not written on prescription vs. multiple strengths and must be designated on prescription)
Vistaril (Hydroxyzine Hydrochloride) (Hydroxyzine Pamoate)	Orthographic	50 mg/mL, 10 mL vial injection solution 25 mg, 50 mg oral capsule 25 mg/5 mL oral solution	25 mg to 100 mg intramuscularly every 4 to 6 hours as needed 50 mg to 100 mg four times daily for children; 50 mg to 100 by mouth daily in divided doses	*Orthographic differences* - 'V'in Vistaril does not resemble 'S' in Safyral when scripted - Safyral has one downstroke vs. Vistaril has no downstrokes *Product characteristic differences* - Strength (single strength, most likely not written on prescription vs. multiple strengths, dose must be desingated on prescription) - Frequency of administration (once daily vs. every 4 to 6 hours as needed)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Sandril (Reserpine) Discontinued, generic forms available in tablets	Orthographic and Phonetic	0.1 mg, 0.25 mg oral tablet	0.1 mg to 1 mg by mouth daily	*Orthographic differences* - Safyral has two downstrokes vs. Sandril has no downstrokes - Safyral has a cross-stroke vs. Sandril has no cross-stroke - Safyral has one letter between the first upstrokes vs. Sandril has two letters between the first upstrokes *Phonetic differecenes* - First syllable of Safyral ”sah”differs from first syllable of Sandril ”San” due to the ’n’ - Safyral has three syllables vs. Sandril has two syllables *Product characteristics differences* - Strength (single strength vs. 0.1 mg or 0.25 mg, must be designated on the prescription)
Sarisol (Butabarital sodium) all products discontinued excpet Butisol Soldium	Orthographic	30 mg, 50 mg oral tablet 30 mg/5 mL oral elixir	- 50 to 100 mg by mouth at bedtime - 15 mg to 30 mg by mouth 3 to 4 times daily - 50 mg to 100 mg 60 to 90 minutes before surgery	*Orthographic differences* - Safyral has two downstrokes vs. Sarisol has no downstrokes - Safyral has three upstrokes vs. Sarisol has two upstrokes *Product characteristics* - Strength (single strength vs. multiple strengths, which must be desiganted on the prescription)
Cafgesic Forte (Acetaminophen, Salicylic acid, Phenyltolox-amine, caffeine)	Orthographic	500 mg/500 mg/20 mg/ 50 mg oral tablet	1 – 2 tablets every 4 to 6 hours as needed for pain	*Orthographic differences* - ’S’ in Safyral does not resemble ’C’ in Cafgesic when scripted - Safyral ends with an upstroke vs. Cafgesic does not *Product characteristic differences* - Frequency (once daily, around the clock vs. every 4 to 6 hours, as needed)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Cal-Gest (Calcium Carbonate)	Orthographic	500 mg chewable oral tablet	1000 mg by mouth per day or 1-2 tablets every 3 to 4 hours for symptoms	*Orthographic differences* - 'S' in Safyral does not resemble 'C' in Cal-gest when scripted - Safyral has a cross-stroke in the middle of the name vs. Cal-gest has a cross-stroke at the end *Product characteristic differences* - Frequency (once daily vs multiple times per day) - Dose (1 tablet vs. if Calgest is taken once daily which is the only overlapping frequency, the dose is two tablets) - Prescription status (requires a prescription vs. over the counter antacid)
Calagel (Diphenhydra-mine Hydrochloride, Zinc Acetate, Menthol and EDTA)	Orthographic	Topical gel	Apply small amount as needed for temporary relief of itching skin	*Orthographic differences* - 'S' in Safyral does not resemble 'C' in Calagel when scripted - Safyral has an upstroke and downstroke next to one another vs. Calagel has one letter in betwen *Product characteristic differences* - Route of administration (oral vs. topical) - Dose (1 tablet vs. small amount) - Dosage form (tablet vs. gel) - Frequency of administration (once daily, around the clock vs. as needed for symptoms)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Cefzil (Cefprozil for oral suspension, USP) (Cefprozil tablets, USP)	Orthographic	125 mg/mL, 250 mg /mL oral suspension 250 mg, 500 mg oral tablets	Adults: 500 mg by mouth every 24 hours as a single dose or divided in two equal doses Pediatric patients: 15 to 30 mg/kg by mouth daily as single or divided dose	*Orthographic differences* - The 'S' in Safyral does not resemble 'C' in Cefzil when scripted - Safyral has seven letters vs. Cefzil has six letters including one letter 'i' which makes it appear shorter in length *Product characteristic differences* - Strength (single strength, most likely not written on prescription vs. multiple strengths, 250 mg and 500 mg and must be designated on prescription) - Dosage form (tablet vs. suspension or tablet, must be designated as such)
SAF-Gel	Orthographic	Topical gel, 3 ounce tube	Apply to wounds as necessary to help with debridement	*Product characteristics* - Route of administration (oral vs. topical) - Dosage form (tablet vs. gel) - Frequency of administration (once daily vs. as needed for wound changes)
Scytera (Coal Tar)	Orthographic	2% topical foam	Apply small amount to affected area 1 to 4 times daily	*Orthgoraphic differences* - Safyral ends w/ an upstroke vs. Scytera does not - Safyral has the downstroke after the cross-stroke vs. Scytera has a downstroke before the cross-stroke *Product characteristic differences* - Route of administraton (oral vs. topical) - Dose (1 tablet vs. small amount) - Dosage form (tablet vs. foam)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Selfemra (Fluoxetine Hydrochloride)	Orthographic	10 mg, 20 mg oral capsule	20 mg by mouth once daily taking continuously or intermittently	*Orthographic differences* - Safyral ends with a upstroke vs. Selfemra does not - Safyral has two upstrokes in the first half of the name vs. Selfemra has three upstrokes in the first half of the name which gives it a different shape *Product characteristics* - Strength (single strength, most likely not written on prescription vs. multiple strengths, 10 mg or 20 mg and must be designated on prescription)
Sufenta (Sufentanil Sitrate)	Orthographic	50 mcg/mL, 1mL, 2 mL, 10 mL ampule	Adults: Up to 8 mcg/kg slow intravenous injection or infusion Children: 10 to 25 mcg/kg intravenous injectin or infusion Epidural dose: 10 mcg to 16 mcg with Bupivicaine 10 mL	*Orthographic differences* - Safyral ends with with an upstroke vs. Sufenta has a letter after the last upstroke *Product characteristic differences* - Route of administraton (oral vs. intravenous or epidural) - Dose (1 tablet vs. weight based regimen of 8 mcg to 25 mcg/kg) - Dosage form (tablet vs. solution)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Sabril (Vigabatrin)	Phonetic	500 mg packet, powder for oral solution 500 mg oral tablet	Infants: 50 mg/kg/day to 150 mg/kg/ day by mouth in divided in two doses Childre: 500 mg to 1500 mg by mouth mixed with water twice daily Adults: 500 mg by mouth twice daily, up to 3 grams a day	*Phonetic differences* - Safyral has three syllables vs. Sabril has two syllables - Second syllable of Safyral is ”fur” or ”fie”vs ”bril” *Product characteristics* - Restricted distribution (retail pharmacy, no restriction vs. Sabril approved with a REMS that requires enrollment of patients and distribution through a specialty pharmacy, therefore Sabril will not enter regular pharmacy channels) - Frequency of administration (once daily vs. twice daily) - Dosage form (tablet vs. available as two different dosage forms, provider would have to designate powder or tablet) - How supplied (4 week pack, written as #1 on outpatient prescription vs. 100 count bottle, written as #60 on Rx)
Soyacal (Soybean oil)	Orthographic	10%, 20% intravenous emulsion	To be used for compounding of total nutrient admixtures, not for direct intravenous administration	*Orthographic differences* - Safyral has three upstrokes vs. Soyacal has two upstrokes - Safyral has a cross-stroke vs. Soyacal has no cross-strokes *Product characteristic differences* - Route of adminsitration (oral vs. intravenous) - Dosage form (tablet vs. emulsion)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet 0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Sulfair-10 Sulfair Forte Sulfair-15 (Sulfacetamide sodium) Generic product Discontinued	Orthographic	10%, 15%, 30% ophthalmic solution	Instill 1 to 2 drops into conjunctival sac(s) of affected eye(s) every 2-3 hours then taper by increasing time intervals	*Orthographic differences* - Safyral ends with an upstroke vs. Sulfair does not end with an upstroke - Safyral does not have consecutive upstrokes vs. Sulfair has two consecutive upstrokes *Product characteristics* - Frequency of administration (once daily vs. every 2-3 hours) - Route of administration (oral vs. eye) - Strength (single strength vs. multiple strengths, must be designated on prescription, 10%, 15%, 30%) - Dosage form (tablet vs.ophthalmic solution)
(b) (4)				

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Saphris (Asenapine Maleate)	Phonetic	5 mg, 10 mg oral tablets	5 mg to 10 mg by mouth twice daily	*Phonetic differences* - Saphryl ends with sound ”fril” vs. Saphris which ends with ”fris” - Saphyral has three syllables, ”saf-a-ral vs. Saphris has two syllables, ”sa-fris” *Product characteristic differences* - Strength (single strength, most likely not written on prescription vs. either 5 mg or 10 mg must be designated on prescription) - Frequency of administration (once daily vs. twice daily)
Sulfoxyl (Benzoyl Peroxide and Sulfur)	Orthographic	Regular: 5%/2% topical lotion Strong: 10%/5% topical lotion	Apply small amoutn once a day to affected area for first week then apply twice daily thereafter.	*Orthgoraphic differences* - Safyral has three upstrokes vs. Sulfoxyl has four upstrokes - Safyral has a down-stroke at the fourth letter vs. Sulfoxyl has a downstroke at the seventh letter and is preceded by a cross-stroke *Product characterisitc differences* - Route of administration (oral vs. topical) - Strength (available as sinlge strength, most likely not written on prescription vs. available in two strengths, particular formulation must be designated)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Cefadyl (Cephapirin Sodium)	Phonetic	500 mg, 1 g, 2 g, 4 g, 20 g lyophilized powder for injection	Adults: 500 mg to 1000 mg intravenously every 4 to 6 hours or 1 g to 2 g intravenously ½ hour to 1 hour prior to surgery Pediatric patients: 40 to 80 mg/kg/day intravenously divided into 4 equal doses	*Phonetic difference* - Safyral first syallable sound is ”sahf’ vs. ”sef” in Cefadyl - Last syllable sound in Safyral is ”ral” vs. ”dil” *Product characterisitc differences* - Route of administration (oral vs. intravenous) - Strength (single strength, most likely not designated on prescription vs. multiple strengths, sepcific dose must be designated) - Frequency of administration (once daily vs. every 4 to 6 hours or prior to surgery)
Sal-Plant (Salicylic acid)	Orthographic	17% topical gel	Apply small amount to affected area as directed	*Orthographic differences* - Safyral has three upstrokes vs. Sal-Plant has four or five upstrokes depending on how scripted - Safyral ends with an upstroke but no cross-stroke vs. Sal-Plant ends with a cross-stroke *Product characteristic differences* - Route of adminsitration (oral vs. topical) - Dose (1 tablet vs. small amount) - Dosage form (tablet vs. gel)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Salagen (Pilocarpine Hydrochloride)	Orthographic	5 mg, 10 mg oral tablet	5 mg by mouth 3 or 4 times a day, titrate up to 10 mg 3 times a day	*Orthographic differences* - Safyral has three upstrokes vs. Salagen has two upstrokes - Safyral ends with an upstroke vs. Salagen does not *Product characterisitc differences* - Frequency of administration (once daily vs. three or four times a day) - Strength (single strength, most likely not designated on prescription vs. multiple strengths, specific strength must be designated on prescription)
Salflex (Salicylic acid)	Orthographic	500 mg oral tablet	3000 mg by mouth in divided doses; 1500 mg twice daily or 500 mg 4 times daily	*Orthographic differences* - Safyral has three upstrokes vs. Salflex has four upstrokes - Safyral ends with a upstroke, but not a cross-stroke vs. Salflex does not end with an upstroke, but does end with a cross-stroke - Safyral has three upstokes distributed equally throughout the name vs. Salflex has all four upstrokes in the first 5 letters *Product characterisitc differences* Frequency of administration (once daily vs. muliptle times per day)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Name confusion is prevented by the stated product characteristics and/or orthographic/phonetic differences as described
Safyral (Drospirenone/ Ethinyl Estradiol/ Levomefolate and Levomefolate)		**3 mg/ 0.03 mg/ 0.451 mg oral tablet** **0.451 mg oral tablet**	**Usual Dose: One tablet by mouth once daily**	
Saljet (Sodium chloride)	Orthgoraphic	30 mL vial sterile saline	Use as needed to moisten wound dressings	*Orthographic differences* - Safyral has a cross-stroke as the third letter vs. Saljet has a cross-stroke as the last letter - Safyral has two letters between the down-stroke and last upstroke vs. Saljet has only one letter between the down-stroke and last upstroke *Product characteristic differences* - Route of administration (oral vs. topical) Frequency of administration (once daily around the clock vs. as needed for wound care) Dosage form (tablet vs. solution)
Sudafed (Pseudoephed-rine)	Orthographic	30 mg, 60 mg, 120 mg, 240 mg oral tablet 15 mg/mL oral soluton	60 mg by mouth every 4 to 6 hours as needed 120 mg by mouth every 12 hours as needed 240 mg by mouth every 24 hours	*Orthographic differences* - Safyral has three upstrokes vs. Sudafed has four upstrokes - Safyral has a cross-stroke as third letter vs. Sudafed has a cross-stroke at the fifth letter *Product characteristic differences* - Strength (single strength, most likely not designated on prescription vs. multiple strengths, must be designated)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22574	ORIG-1	BAYER CORP PHARMACEUTICAL DIV	YASMIN PLUS (DEOSPIRENONE ETHINYL ESTRAD

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

/s/

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