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:	September 22, 2010
Application Type/Number:	NDA 022504
Through:	Melina Griffis, RPh, Team Leader Denise Toyer, Pharm.D., Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Irene Z. Chan, Pharm.D., BCPS, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Axiron (Testosterone) Solution, 2%
Application Type/Number:	NDA 022542
Applicant:	Kendle International, Inc.
OSE RCM #:	2010-1264

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

CONTENTS

1 INTRODUCTION

This re-assessment of the proprietary name responds to a notification that NDA 022504 may be approved within 90 days. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Axiron, acceptable in OSE Review #2010-343, dated May 4, 2010.

The Division of Reproductive and Urology Products did not have any concerns with the proposed name, Axiron, and the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective as noted in OSE Review #2010-343.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff searched 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 that were used in OSE Review #2010-343 for the proposed proprietary name, Axiron. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. 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 searches of the databases yielded no new names thought to look or sound similar to Axiron and represent a potential source of drug name confusion. DMEPA staff also did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name Axiron, as of September 10, 2010.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Axiron, is not vulnerable to name confusion that can lead to medication errors nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Axiron, 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 Urology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

1. **OSE review #2010-343 Proprietary Name Review of Axiron; Chan, Irene Z.**

2. ***Drugs@FDA (***[*http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm*](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/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml*](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.

4. ***Division of Medication Error Prevention and Analysis proprietary name 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.

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

/s/

IRENE Z CHAN
09/22/2010

DENISE P TOYER on behalf of MELINA N GRIFFIS
09/22/2010

DENISE P TOYER
09/22/2010

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

Date:	May 4, 2010
To:	Scott Monroe, MD, Director Division of Reproductive and Urology Products
Through:	Melina Griffis, RPh, Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Irene Z. Chan, Pharm.D., BCPS, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Axiron (Testosterone) Solution, 2%
Application Type/Number:	NDA 022504
Applicant/Applicant:	Kendle International, Inc.
OSE RCM #:	2010-343

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CONTENTS

EXECUTIVE SUMMARY

This review evaluates the acceptability of the proposed proprietary name Axiron from a safety and promotional perspective based on the product characteristics provided by Kendle International, Inc. DMEPA concludes the proposed proprietary name, Axiron, is acceptable. The Applicant will be notified by letter, and the proposed proprietary name must be re-evaluated 90 days prior to approval of the NDA.

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 responds to a request from Kendle International, Inc. dated February 3, 2010, for an assessment of the potential for confusion of the proposed proprietary name, Axiron, with other proprietary or established drug names in the usual practice settings. The Applicant submitted an external study conducted by (b) (4)) in support of their proposed proprietary name. Kendle also submitted labels and labeling for review as part of the original NDA application which are reviewed under separate cover (OSE Review # 2010-367).

1.2 REGULATORY HISTORY

DMEPA reviewed the proposed proprietary name, Axiron, during the IND stage and found the name conditionally acceptable. We refer you to OSE Review # 2009-691 dated September 18, 2009.

1.3 PRODUCT INFORMATION

Axiron is the proposed proprietary name for Testosterone Solution 2%, a non-sterile solution for transdermal administration to the axilla. This drug will be listed as a Schedule III Controlled Substance according to the Federal Controlled Substances Act. The Applicant is seeking approval for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary Hypogonadism (Congenital or Acquired) – testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone levels and gonadotropins (FSH, LH) above the normal range.
- Hypogonadotropic Hypogonadism (Congenital or Acquired) – idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum levels but have gonadotropins in the normal or low range.

The doses proposed for marketing authorization are 30 mg, 60 mg, 90 mg, and 120 mg.

Table 1: Proposed Axiron Dosage and Administration

Testosterone Dose	Volume Applied	Number of Pumps	Application
30mg	1.5mL	1	Applied daily by 1 pump/dose to one axilla (1.5mL to one axilla)
60mg	3.0mL	2	Applied daily by 2 pumps/doses to the axilla (1.5mL to each axilla)
90mg	4.5mL	3	Applied daily by 3 pumps/doses to the axilla (1.5mL to each axilla, followed by a further 1.5mL to one axilla)
120mg	6.0mL	4	Applied daily by 4 pumps/doses to the axilla (1.5mL to each axilla, followed by a further 1.5mL to each axilla)

Axiron is applied to the skin surface of the axilla by use of a hand held applicator once daily at approximately the same time each day. Axiron will be supplied as a single bottle containing 110 mL of product, capable of dispensing 60 x 1.5 mL metered doses. The bottle is fitted with a metered dose pump, and an applicator with a protective cap. All components are designed to be disposed once finished. Axiron should be stored at room temperature.

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, 2.3, and 2.4 identify specific information associated with the methodology for the proposed proprietary name Axiron.

2.1 SEARCH CRITERIA

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

To identify drug names that may look similar to Axiron, 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 (6 letters), upstrokes (1, capital 'A'), downstrokes (none), cross strokes (1, lower case 'x'), and dotted letters (1, lower case 'i'). Additionally, several letters in Axiron 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 Axiron.

When searching to identify potential names that may sound similar to Axiron, the DMEPA staff search for names with similar number of syllables (three), stresses (AX-i-ron, ax-I-ron, ax-i-RON), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (see Appendix B). The Applicant's intended pronunciation (axe-e-ron) was also taken into consideration, as it was included in the Proprietary Name Review Request. Furthermore,

[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)

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. Axiron Study (conducted on February 26, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: Axiron 60 mg once daily	Axiron 120 mg #1 a month supply
Outpatient Prescription: Axiron 120 mg @daily One month supply	

2.3 NAME SIMILARITY RISK ASSESSMENT POLL

To further assist in determining the overall risk of confusion between Axiron and one specific name (Avinza), the reviewing safety evaluator conducted a poll of the DMEPA staff to determine if they had concerns with the orthographic and/or phonetic similarity of these two names. The poll questions are listed in Appendices D and E.

2.4 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

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

After the Safety Evaluator has determined the overall risk associated with the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's

risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA database searches yielded a total of 30 names as having some similarity to the name Axiron. However, 17 of the 30 names were previously evaluated in OSE Review # 2009-691 and found not to be vulnerable to confusion with Axiron. Additionally, one name (Axion) is a discontinued foreign drug, and therefore, will not be evaluated. Thus, the database and information sources searched yielded a total of 12 new names.

Nine of the twelve names were thought to look like Axiron. These include Arava, Asbron, Avinza, Avita, Avitene, Cleocin, Crixivan, Lanoxin, and Ultrona. The remaining three names, Atryn, Axon, and (b) (4) were thought to look and sound similar to Axiron.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of February 19, 2010.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the 12 new names identified by DMEPA staff (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Axiron.

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 48 practitioners responded to the FDA prescription analysis studies. Only 23 of the practitioners interpreted the name correctly as "Axiron". Four providers misinterpreted the name Axiron as (b) (4) in the verbal prescription study, replacing the "i" with an "e." (b) (4) Additionally, the infix "ir" was misinterpreted as "n" in six instances in the written inpatient prescription studies. One practitioner misinterpreted Axiron as Axid in the inpatient prescription study and one provider misinterpreted Axiron as Aceon in the verbal prescription study. Aceon and Axid are both marketed products that were previously evaluated in OSE Review # 2009-691 and found not to be vulnerable to confusion with Axiron; however, we will re-evaluate these names. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

The proprietary name risk assessment submitted by the Applicant found the name acceptable. Their evaluator identified a total of nine drug names thought to have some potential for confusion with the name Axiron: Aceon, Apexicon, Aspirin, Axert, Axid, Exelon, Iron, Maxitrol, and Pacerone. Eight of the nine names were previously evaluated in OSE Review # 2009-691 and found not to be vulnerable to confusion with Axiron. However, in our recent prescription studies, two of these eight names were confused as the proposed name; therefore, these two names, Aceon and Axid, will be re-evaluated. The remaining name, Exelon, was also identified by DMEPA during the database searches.

3.5 SAFETY EVALUATOR RISK ASSESSMENT OF PROPOSED PROPRIETARY NAME

The primary Safety Evaluator identified 19 additional names which were thought to look or sound similar to Axiron and represent a potential source of drug name confusion.

The names identified by the primary Safety Evaluator to have look-alike similarities are Afaxin, AK-Con, Akurza, Ancrod, Anurx, Atarax, Avenoc, (b) (4), Ceresin, (b) (4), Fluarix, Oncovin, (b) (4), Spiriva, and (b) (4). One name, (b) (4), was thought to have look-alike and sound-alike similarity.

A total of 33 names were identified for their similarity to Axiron from the combined searches: 19 identified by the primary safety evaluator, 2 identified in the FDA prescription analysis studies, and 12 identified in section 3.1 above.

3.6 NAME SIMILARITY RISK ASSESSMENT POLL

Eleven DMEPA staff members responded to the poll conducted on March 25, 2010, which asked, "Is the name Avinza convincingly similar to Axiron such that practitioners would become confused at any point in the usual practice setting (yes or no)? Why or why not? Please provide your rationale." Five of the eleven participants responded "Yes". One participant was unsure. Five of the eleven participants responded "No". The comments provided by the participants are included in Appendix D. The medication error staff that responded "yes" or were unsure were given the product characteristics of Axiron and Avinza along with a follow up question which was "If you believe the names are convincingly similar, could confusion between Axiron and Avinza conceivably result in medication errors in the usual practice setting (Yes or No)? Why or why not? Please provide your rationale." Six participants responded to this part of the poll conducted March 26, 2010. Two out of the six participants responded "Yes" and the remaining four responded "No". The two who stated "Yes" believed the shared dosing frequency and overlap in doses (30 mg, 60 mg, 90 mg, and 120 mg) would increase the likelihood of a medication error to occur. However, one of the participants questioned whether prescribers would dose Axiron in pumps or milligrams. The four participants who answered "No" believed that differences in route of administration and dosage form minimized the risk of error. In addition, one participant noted that an Axiron order would more than likely include the descriptor "apply". Another participant noted that doses will likely be written in terms of pumps or applications rather than milligrams. See Appendix E for details.

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

3.7.1 Initial Phase of Review

In a response to the OSE February 22, 2010, e-mail, the Division of Reproductive and Urology Products (DRUP) did not have any objections to the proposed proprietary name, Axiron.

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

3.7.2 Midpoint of Review

On March 31, 2010, DMEPA notified the Division of Reproductive and Urology Products via e-mail that we had objections to the proposed proprietary name, Axiron. Per e-mail correspondence from DRUP on March 31, 2010, they indicated that there were no reported concerns with our assessment of the proposed proprietary name, Axiron.

4 DISCUSSION

This proposed name, Axiron, was evaluated from a safety and promotional perspective. Furthermore, input from pertinent disciplines involved with the review of this application was considered accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and the Division of Reproductive and Urology Products concurred with the findings of the promotional assessment.

4.2 SAFETY ASSESSMENT

In total, 33 names were evaluated by DMEPA. Eighteen of the 31 names were eliminated for the following reasons (see Appendices F, G, H, I, and J): 7 of the 18 names lacked convincing orthographic and/or phonetic similarity to the proposed proprietary name Axiron, 11 other names did not undergo failure mode and effect analysis (FMEA) because they were either not drugs, products not marketed in the U.S., proposed proprietary names found unacceptable by DMEPA, proposed proprietary names for products later approved under a different proprietary name, proposed proprietary names for NDA applications that were withdrawn or not submitted, or a name which had limited product characteristic information.

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 15 names and lead to medication errors. Although two names were confused as the proposed proprietary name in our prescription studies, Aceon and Axid, we determined that name confusion is prevented by a combination of product characteristics, such as different usual doses, dosage forms, and route of administration, and orthographic differences. See Appendix K for more information.

We conducted a risk assessment poll to further assist in determining the overall risk of confusion between Axiron and Avinza. The majority of respondents ultimately determined that confusion between Axiron and Avinza would not conceivably result in medication errors in the usual practice setting, and our analysis concurred with the majority opinion. Our analysis determined that orthographic differences in the names Axiron and Avinza, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. See Appendix L for more information.

This analysis determined that the name similarity between Axiron was unlikely to result in medication errors with any of the 15 products for the reasons presented in Appendices K and L. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Axiron, is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Axiron, for this product at this time. Our analysis is consistent with the external risk assessment conducted by (b) (4) that was provided by the Applicant. The Applicant will be notified via letter.

5.1 COMMENTS TO THE APPLICANT

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

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

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.

6 REFERENCES

1. Adverse Events Reporting System (AERS)

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

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

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

3. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

5. 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.

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

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

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

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

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

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

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

Provides information regarding patent and trademarks.

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

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

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

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

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

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

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

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

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

List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

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

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

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

17. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions

APPENDICES

Appendix A:

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 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

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[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.

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

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.

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 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

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

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)].

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, Axiron	Scripted may appear as	Spoken may be interpreted as
Capital 'A'	Ce, Ci, Cl, Fl, O, s, or U	Any vowel
lower case 'a'	ce, ci, cl, e, o, or u	Any vowel
lower case 'x'	f, k, n, p, r, t, v	z
lower case 'i'	c, e	any vowel
lower case 'ir'	n, u	er
lower case 'r'	n, v, x	
lower case 'o'	a, e, or u	any vowel
lower case 'n'	m, r, s, x	

Appendix C: FDA Prescription Study Responses

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
axid	Axiron	(b) (4)
Axiron	axiron	(b) (4)
Axiron	Axiron	Exceron
Axiron	Axiron	Aceon
Axnon	Axiron	(b) (4)
Axuron	Axiron	Exceron
Axiron	Axiron	Exeron
Axnon	Axiron	Exeron
Axiron	Axiron	Exteron
Axnon	Axiron	(b) (4)
Axiron	Axiron	Axuron
Axnon	Axiron	Xeron
Axinon	Axiron	Axuron
Axnon	Axiron	Exeron (14)
Axran	Axiron	
Axnon (16)	Axiron	
	Axiron	
	Axicron (18)	

Appendix D: Safety Evaluator Poll Responses (Similarity) - Axiron vs. Avinza

Poll Question	Is the name Avinza convincingly similar to Axiron such that practitioners would become confused at any point in the usual practice setting (yes or no)? Why or why not? Please provide your rationale.	Why or Why Not?
Staff Responses	Yes	Yes, I feel the names are similar because: -same length -share beginning letter A and third letter -the first 4 letters appear similar when scripted ('x' can look like 'v' if not crossed all the way and the 'r' and 'n' can look similar -z can be written without the downstroke and ending letters can be trailed off.
	Yes	I would have to say yes, they can be confused. These are six letter names beginning with the letter A. The remaining five letters may not provide any upstroke or down stroke (z written without a down stroke). The cross stroke from the 'x' is the only distinguishing feature which may be overlooked.
	Yes	Yes. All the letters are orthographically similar to each other when scripted.
	Yes	Yes, although these two names do not sound alike, most of the letters in each name can be written to look similar.
	Yes.	Yes. Both names begin with capital letter 'A.' Also, 'vi' can look like 'xi' and if the 'z' is not scripted with a downstroke, it can look like an 'r' and 'a' can look like 'o.'
	Unsure	I'm on the border. Maybe if there are overlapping product characteristics, but no if there aren't. My samples don't really look alike but I can see potential since there is no upper/lower case to distinguish them.
	No	No. I do not think they are orthographically or phonetically similar enough to be confused.
	No	No even though the first part of the name looks very similar (avin and axir) when scripted. The last two letters in each of the name provide the differentiation. Both the names contain 6 letters, however, when scripted Axiron appears to be a little longer than Avinza.

	No	No. I don't think the names are convincingly similar. The letter "z" in Avinza (when scripted with a downstroke) and the letter "x" in Axiron help to differentiate the names. Also, when I look at the names in their entirety, they just don't look very similar to me.
	No	I do not think that the name Avinza is convincingly similar to Axiron such that practitioners would become confused at any point in the usual practice setting. Although both names contain six letters, and beginning of each name may appear similar when scripted ("avi-" vs. "axi-"), the endings appear different ("nza" vs. "ron") when scripted.
	No	I do not think these two names are convincingly similar when written because the cross-strokes (e.g. "z" in avinza and "x" in Axiron) appear in different locations within their names. Stated another way, I think the appearance of the "x" (in Axiron) early in the name may adequately distinguish this name from Avinza. My assumption is that the "z" (in Avinza) is not written as a down-stroke, in which case, it would be a more obvious distinguishing factor.

Appendix E: Safety Evaluator Poll Responses (Medication Errors) - Axiron vs. Avinza

Poll Question	If you believe the names are convincingly similar, could confusion between Axiron and Avinza conceivably result in medication errors in the usual practice setting (Yes or No)? Why or why not? Please provide your rationale.	Why or Why Not?
Staff Responses	Yes	If Axiron will be dosed according to 'x mg' versus 'x number of pumps' there could be dose overlap between Axiron and Avinza, in which case, the orthographic similarities coupled with these product characteristic overlaps, are significant enough that they could lead to wrong drug medication errors. i.e. Axiron 30 mg once daily Avinza 30 mg once daily Do you have a sense of how prescribers would dose Axiron (X pumps versus mg)? That might help determine the significance of the overlap. If not, I believe you'd have to make your determination based on the fact that the doses do overlap in milligrams.

	Yes	Yes because multiple dosage strengths overlap (30 mg, 60 mg, 90 mg, and 120 mg) and both are administered once a day.
	No	I don't think so since sig will be different and DF/ROA is different too.
	No	No because of differences in DF (solution vs. tablet), ROA (topical vs. oral), and strength (2% vs. 30 mg, etc.).
	No	No, the product characteristics of strength (omission possible as it is a single strength product), dosage form, and route of administration will likely minimize confusion. Although the mg doses of both products overlap, doses for the patient will likely be written in terms of pumps/applications rather than milligrams.
	No	My answer is no. Even though the strengths and frequency of administration overlap, the route of administration differs. The Axiron order would more than likely have a descriptor such as "apply", a location would like be given on where to apply and the number of pumps will need to be specified if it's more than one. Although the names look similar to me, depending on how they are scripted they could look different. So even though I see similarities in the names, the product characteristics are different enough for me that I do not think an error would occur.

Appendix F: Drug names that lack convincing orthographic and/or phonetic similarities

Name	Similarity to Axiron
Asbron	Look alike
Atryn	Look alike and sound alike
Avita	Look alike
Avitene	Look alike
Cleocin	Look alike
Lanoxin	Look alike
Ultrona	Look alike

Appendix G: Product that is not a drug

Name	Similarity to Axiron	Product Description
Ceresin	Look alike	This is a substitute for beeswax that can be used in compounding.

Appendix H: Names of products withdrawn from the market or not marketed in the U.S.

Proprietary Name	Similarity to Axiron	Status
Afaxin (Vitamin A Palmitate)	Look alike	Product discontinued with no therapeutic equivalents available. This product was previously marketed as a 50,000 unit oral capsule.
Oncovin (Vincristine Sulfate)	Look alike	Product discontinued with no therapeutic equivalents available. This product was previously marketed as an injectable formulation.

Appendix I: Unapproved proprietary names

Proprietary Name	Similarity to Axiron	Status and Date
		(b) (4)

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

Proprietary Name	Similarity to Axiron	Status and Date
		(b) (4)

Appendix J: Names which have limited product characteristic information

Proprietary Name	Similarity to Axiron	Comments
Anurx	Look alike	Name found in Facts and Comparisons, but no active ingredients listed. More detailed product characteristics could not be found in Micromedex, Lexi-Comp, Drugs@FDA, Clinical Pharmacology On-line, Redbook, Natural Medicines Database, or Stat-Ref

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

Appendix K: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Axiron	Strength	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Axiron (Testosterone) Solution	**N/A**	**2%**	**30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 actuation pumps or 1.5 – 6 mLs) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day or Apply X mL under each arm once a day.**	**N/A**
Aceon (perindopril erbumine) Tablets	Look alike	2 mg, 4 mg, 8 mg	8 mg once daily or in two divided doses. Can increase up to a maximum of 16 mg per day.	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Orthographic: *The letter string 'xir' in Axiron looks different from the corresponding letter string 'ceo' in Aceon.* Usual Dose: *30 mg, 60 mg, 90 mg, 120 mg or X pumps or X mL vs. 8 mg once daily or 4 mg twice daily* Route of Administration: *Transdermal application to axilla vs. oral* Dosage Form: *Solution for transdermal administration vs. tablet*
AK-Con (naphazoline hydrochloride) Ophthalmic Solution	Look alike	0.1%	1-2 drops in the conjuntival sac(s) every 3-4 hours as needed	Route of Administration: *Transdermal application to axilla vs. ophthalmic* Usual Dose: *30 mg, 60 mg, 90 mg, 120 mg, or X pumps or X mL vs. one to two drops* Strength: *2% vs. 0.1%* Frequency: *Once daily vs. every 3 – 4 hours as needed*

Product name with potential for confusion	Similarity to Axiron	Strength	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Axiron (Testosterone) Solution	**N/A**	**2%**	**30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 actuation pumps or 1.5 – 6 mLs) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day or Apply X mL under each arm once a day.**	**N/A**
Akurza (salicylic acid) Cream or Lotion	Look alike	6%	Apply thin film sparingly once daily at bedtime or as directed	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Orthographic: *When scripted, Axiron contains no downstrokes in the suffix whereas Akurza may contain the downstroke "z". In addition, the suffix "-on" does not look like "-za" when scripted.* Usual Dose: *30 mg, 60 mg, 90 mg, 120 mg or X pumps or X mL vs. a thin film/layer* Dosage Form: *Solution for transdermal administration vs. cream or lotion (prescriber would have to specify one or the other)* Usage: *Preliminary usage data indicates Akurza is not commonly prescribed. Therefore, low use minimizes the potential confusion between Akurza and Axiron*
Ancrod (established name for ViprinexTM) Injectable	Look alike	NA	0.167 IU/kg/hr over 2-3 hours	Route of Administration: *Transdermal application to axilla vs. intravenous infusion* Dosage Form: *Solution for transdermal administration vs. injectable* Setting of Use: *Ancrod is used in emergency settings for cardiothoracic bypass or acute ischemic stroke*

Product name with potential for confusion	Similarity to Axiron	Strength	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Axiron (Testosterone) Solution	**N/A**	**2%**	**30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 actuation pumps or 1.5 – 6 mLs) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day or Apply X mL under each arm once a day.**	**N/A**
Arava (leflunomide) Tablet	Look alike	10 mg, 20 mg, 100 mg	20 mg daily	Route of Administration: *Transdermal application to axilla vs. oral* Strength / Usual Dose: *There is no numerical overlap in strength or usual dose for these products* Dosage Form: *Solution for transdermal administration vs. tablet*
Atarax (hydroxyzine hydrochloride) Tablet or Syrup	Look alike	Syrup: 10 mg/5 mL Tablet: 10 mg, 25 mg, 50 mg, 100 mg	Pruritis: Take 25 mg three times daily Symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested: 50 – 100 mg four times daily	Route of Administration: *Transdermal application to axilla vs. oral* Strength / Usual Dose: *There is no numerical overlap in strength or usual dose for these products* Dosage Form: *Solution for transdermal administration vs. tablet or syrup* Frequency: *Once daily vs. 3 – 4 times daily*
Avenoc (Aesculus hippocastanum, Collinsonia Canadensis, hamamelis virginiana) Ointment or Suppositories	Look alike	NA	Ointment: Apply thin layer externally to the affected area up to 4 times a day Suppository: Insert suppository rectally morning and night	Usual Dose: *30 mg, 60 mg, 90 mg, 120 mg or X pumps or X mL vs. a thin layer or one suppository* Frequency: *Once daily vs. 2 - 4 times daily* Dispensing Setting: *Avenoc is a homeopathic medicine available over the counter and will not likely be dispensed pursuant to a prescription.* Schedule: *CIII vs. a non-controlled substance*

Product name with potential for confusion	Similarity to Axiron	Strength	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Axiron (Testosterone) Solution	**N/A**	**2%**	**30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 actuation pumps or 1.5 – 6 mLs) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day or Apply X mL under each arm once a day.**	**N/A**
Axid (Nizatidine) Capsule or Oral Solution	Look alike	Oral Solution: 15 mg/mL Capsule: 150 mg, 300 mg	150 mg once or twice daily or 300 mg once daily at bedtime depending on indication.	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Orthographic: *Axiron contains six letters whereas Axid contains four letters. When scripted, Axiron appears longer than Axid.* *Axiron contains no upstrokes whereas Axid contains the upstroke "d"..* Route of Administration: *Transdermal application to axilla vs. oral* Usual Dose: *30 mg, 60 mg, 90 mg, 120 mg or X pumps or X mL vs. 150 mg or 300 mg* Dosage Form: *Solution for transdermal administration vs. Capsule or oral solution*
Axon (phenylephrine hydrochloride and chlorpheniramine maleate) Capsule	Look alike and sound alike	20 mg/4 mg	NA	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Orthographic: *Axiron contains six letters whereas Axon contains four letters. When scripted, Axiron appears longer than Axon.* *Axiron contains three syllables whereas Axon contains two syllables.*

Product name with potential for confusion	Similarity to Axiron	Strength	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Axiron (Testosterone) Solution	**N/A**	**2%**	**30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 actuation pumps or 1.5 – 6 mLs) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day or Apply X mL under each arm once a day.**	**N/A**
				Route of Administration: *Transdermal application to axilla vs. oral* Strength / Usual Dose: *There is no numerical overlap in strength or usual dose for these products* Dosage Form: *Solution for transdermal administration vs. Capsule*

(b) (4)

[redacted]

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

Product name with potential for confusion	Similarity to Axiron	Strength	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Axiron (Testosterone) Solution	**N/A**	**2%**	**30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 actuation pumps or 1.5 – 6 mLs) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day or Apply X mL under each arm once a day.**	**N/A**
Crixivan (indinavir sulfate) Capsule	Look alike	100 mg, 200 mg, 333 mg, 400 mg	800 mg by mouth every 8 hours	Route of Administration: *Transdermal application to axilla vs. oral* Strength / Usual Dose: *There is no numerical overlap in strength or usual dose for these products* Dosage Form: *Solution for transdermal administration vs. Capsule* Frequency: *Once daily vs. three times daily every 8 hours*
Fluarix (influenza virus vaccine) Injection	Look alike	NA	0.5 mL intramuscular injection one time	Route of Administration: *Transdermal application to axilla vs. intramuscular injection* Dosage Form: *Solution for transdermal administration vs. injection* Frequency: *Once daily vs. one time*
Spiriva (tiotropium bromide monohydrate) Capsules for Respiratory Inhalation	Look alike	0.018 mg / inhalation	2 inhalations once daily of one capsule	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Orthographic: *The suffix –iva does not look similar to the suffix –ron. Additionally, Axiron does not contain a downstroke, whereas Spiriva contains one downstroke "p".* Route of Administration: *Transdermal application to axilla vs. oral inhalation*

Product name with potential for confusion	Similarity to Axiron	Strength	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Axiron (Testosterone) Solution	**N/A**	**2%**	**30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 actuation pumps or 1.5 – 6 mLs) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day or Apply X mL under each arm once a day.**	**N/A**
				Strength / Usual Dose: *There is no numerical overlap in strength or usual dose for these products* Dosage Form: *Solution for transdermal administration vs. capsule for inhalation*

Appendix L: Potentially confusing names with overlap in strength

Proposed Name: **Axiron (Testosterone) Solution**	**Strength:** **2%**	**Usual Dose and Administration:** **30 mg, 60 mg, 90 mg, or 120 mg (1 – 4 pumps) applied once daily to the axilla. Usual sig may be: Apply X pumps under each arm once a day or Apply X mg under each arm once a day.**
Failure Mode: Name confusion	**Causes (can be multiple)**	**Prevention of Failure Mode**
Avinza (morphine sulfate) Extended-release Capsule **Strengths:** 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, 120 mg **Usual Dose:** Dose varies but is administered once daily; maximum dose is 1600 mg per day	**Orthographic Similarities:** Both names begin with the letter 'A'. Additionally, 'vin' can look like 'xir' when scripted. **Overlap in Dose:** May have overlap in 30 mg, 60 mg, 90 mg, or 120 mg dose. **Overlap in Frequency**: Both products are dosed once daily.	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. **Rationale:** When scripted, Axiron contains no downstroke in the suffix whereas Avinza may contain the downstroke "z". Additionally, the suffix "-on" does not look like "-za" when scripted. Avinza is a capsule that is administered orally whereas Axiron is a solution that is administered topically to the axilla. Therefore, these two products have different dosage forms and different routes of administration. A prescription written for Axiron would likely include instructions to "apply" the medication and may also include instruction to "apply to the axilla", which would help to differentiate it from Avinza. Avinza is a schedule II controlled substance. Due to federal regulations, any prescription for Avinza requires a defined quantity to dispense such as "30 capsules" or "#30". Axiron will likely be ordered in a quantity of "1 bottle" or "110 mL". This difference should alert a provider if there is a question regarding what medication to dispense.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22504	ORIG-1	ACRUX PHARMA PTY LTD	TESTOSTERONE

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