CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-201s000

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:	December 29, 2009
To:	Norman Stockbridge, MD, Director Division of Cardiovascular and Renal Products
Through:	Laura Pincock, PharmD, Acting Team Leader Denise Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Shirley Zeigler, MSN, CRNP, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Asclera (Polidocanol) Injection 0.5 % (10 mg/2 mL) and 1% (20 mg/2 mL)
Application Type/Number:	NDA 021201
Applicant/Applicant:	Chemische Fabrik Kreussler & Co., GmbH
OSE RCM #:	2009-1870

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EXECUTIVE SUMMARY

Asclera is the proposed proprietary name for Polidocanol Injection. 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 Asclera acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

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

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Chemische Fabrik Kreussler & Co., GmbH on September 30, 2009, for an assessment of the proposed proprietary name, Asclera, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The Applicant also submitted container labels and carton labeling for review, which will be in a separate review (OSE Review #2009-2241).

1.2 REGULATORY HISTORY

Asclera (Polidocanol) is currently under review by the Division of Cardiovascular and Renal Products under NDA 21201 with a PDUFA goal date of January 10, 2010. The Applicant initially submitted the proprietary name (b) (4) for review (OSE Review #2009-973), but during the initial steps in the proprietary name review process, the Division of Drug Marketing, Advertising, and Communications (DDMAC) did not recommend the proposed name, (b) (4) . The Applicant subsequently submitted the proprietary name Asclera.

1.3 PRODUCT INFORMATION

Asclera (Polidocanol Injection) is indicated for the sclerosing of spider veins (or very small varicose veins) and reticular veins (small varicose veins). The usual dose is 0.1 mL-0.3 mL slowly injected locally into the vasculature to be sclerosed. The 0.5% concentration is indicated for spider veins, (b) (4) and very small varicose veins, and the 1% concentration is indicated for reticular varices and small varicose veins. The frequency of use is up to 16 injections at multiple sites per treatment day in spider veins and up to 8 injections at multiple sites per treatment day in reticular veins. One or more repeat treatments may be necessary for optimal outcome, depending on the extent of the varicose veins. These treatments should be separated by one or two weeks.

Asclera is proposed to be marketed in 2 mL ampules of the 0.5% (10 mg/2 mL) and 1% (20 mg/2 mL) concentrations, in packages of 5 ampules which 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 and 2.2 identify specific information associated with the methodology for the proposed proprietary name, Asclera.

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 Asclera, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (7 letters), upstrokes (two, capital letter 'A' and lowercase letter 'l'), down strokes (none), cross strokes (none), and dotted letters (none). Additionally, several letters in Asclera may be vulnerable to ambiguity when scripted, including the capital letter 'A' may appear as 'O' or 'I' and to lower case pairs 'ce', 'cl', 'ci'; lower case 's' may appear as lower case ''r', 'n' or 'o'; lower case "c" may look like lower case 'a', 'o', or 'e'; lower case letter 'l' may appear as lower case 'b', 'e', or 'f'; lower case 'e' may look like lower case 'a', 'o' or 'c'; lower case 'r' may look like lower case 'n', 'x', 'h', or 'm'; and lower case 'a' may look like lower case 'e', 'o', or 'c'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Asclera.

When searching to identify potential names that may sound similar to Asclera, the DMEPA staff searches for names with similar number of syllables (3), stresses (AS-cler-a; as-CLER-a; as-cler-A), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'As' may sound like 'Is' or 'Es'; 'scl' may sound like 'sk'; 'sclera' may sound like 'sclero'; 'era' may sound like 'ara'; and 'ra' may sound like 'ro' or 'raw'. The Applicant's intended pronunciation (as' kler a) was also taken into consideration, as it was included in the Proprietary Name Review Request. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

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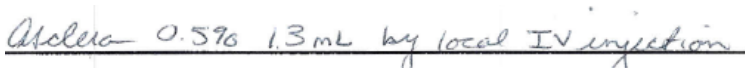
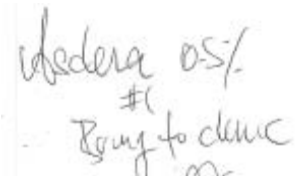
[1] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

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

Figure 1. Asclera Study (conducted on October 23, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	Asclera 0.5% Dispense: # 5 Use as directed Bring to Clinic
Outpatient Medication Order: 	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of nineteen names as having some similarity to the name Asclera.

Thirteen of the nineteen names (Aclaro, Acular, Allegra, Alora, Arduan, Aredia, Asacol, Ascendin, Ceclor, Dulera, Excella, Oscion, and Sclerosal) were thought to look like Asclera. The remaining six names (Aldara, Antara, Ascarel, (b) (4), Asclor, and Sclera), were thought to look and sound similar to Asclera.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of December 11, 2009.

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 Asclera.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of twenty-three practitioners responded in the prescription analysis studies. Thirteen of the participants interpreted the name correctly as "Asclera," with correct interpretation occurring in both the inpatient written and voice studies. The remainder of the written responses misinterpreted the drug name. The majority of misinterpretations occurred with the initial capital letter 'A' being misinterpreted as 'I'. In the outpatient written studies, the name Asclera, was misspelled 100% of the time. The majority of misinterpretations occurred with the initial letters 'A' being misinterpreted as 'I' and lower case 'cl' misinterpreted as 'd'. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

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

3.4.1 *Initial Phase of Review*

In a response to the OSE October 14, 2009 e-mail, the Division of Cardiovascular and Renal Products (DCRP) did not object to the proposed proprietary name, Asclera.

3.4.2 *Midpoint of Review*

On November 18, 2009 DMEPA notified the Division of Cardiovascular and Renal Products (DCRP) via e-mail that we had no objections to the proposed proprietary name Asclera. Per e-mail correspondence from the Division of Cardiovascular and Renal Products on November 30, 2009, they indicated that they concur with our assessment of the proposed proprietary name, Asclera.

3.5 COMMENTS FROM THE DIVISION OF ANTI-INFECTIVE AND OPHTHALMOLOGY (DAIOP)

On November 4, 2009, DMEPA asked DAIOP whether there were any concerns with the name, Asclera because it contains the word 'sclera'. Sclera is a term for the white part of the eye. The Division of Anti-Infective and Ophthalmology Products replied via e-mail on November 4, 2009, that the proprietary name, Asclera, was unlikely to result in medication errors.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified four additional names (Aralen, Astelin, Estar, and Acilac) which were thought to look similar to Asclera and represent a potential source of drug name confusion.

Thus, we evaluated a total of twenty-three names for their similarity to the proposed name.

4 DISCUSSION

Neither DDMAC, the Division of Cardiovascular and Renal Products, nor the Division of Anti-Infective and Ophthalmology Products had concerns with the proposed name Asclera.

A total of twenty-three names were identified and evaluated by DMEPA. Twelve of the twenty-three names lacked convincing orthographic and/or phonetic similarity to the proposed proprietary name Asclera and were not evaluated further. (see Appendix C).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining eleven names and lead to medication errors. This analysis determined that the name similarity between Asclera was unlikely to result in medication errors with any of the twelve products for the reasons presented in Appendices D through H. Additionally, no other sources of confusion were identified by DMEPA.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Asclera, 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, Asclera, 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. 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 Nina Ton, OSE project manager, at 301-796-1648.

5.1 COMMENTS TO THE APPLICANT

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

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

REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

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

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

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

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

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

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

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

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly 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 Error Prevention and Analysis (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND Review Division or Generic drugs

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

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

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

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or

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

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

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

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

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

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

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

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

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

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

Appendix B: **FDA Prescription Study Responses.**

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Asclera	Asdera	Asclera
Asclera	Isdera	Asclara
Asclera	Isdera	
Aldero	Asdera	
Arclera	Isdera	
Asclera	Asdera	
	Isdera	
	Isdera	
	Isdera	
	Asdera	
	Asdera	
	Asdera	
	Isclera	
	Asdera	
	Asdera	

Appendix C: Drug names lacking convincing look or sound-alike similarities to Asclera

Name
Acilac
Allegra
Alora
Arduan
Asacol
Ascendin
Astelin
Dulera
Estar
Excella
Oscion
Sclerosal

Appendix D: Products which are not a drug

Name	Similarity to Asclera	Description
Sclera	Look and sound-alike	The **sclera**, also known as the ***white part of the eye***, is the opaque (usually white, though certain animals, such as horses and lizards, can have black sclera), fibrous, protective, outer layer of the eye containing collagen and elastic fiber.

Appendix E: Names of products marketed or trademarketed in foreign countries

Name	Similarity to Asclera	Country
Asclor (Chloramphenicol)	Look and Sound-alike	India

Appendix F: Product names that have not ever been approved

Proprietary Name	Similarity to Asclera	Status of product name
(b) (4)	Look and Sound-alike	(b) (4)

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

Appendix G: Products with no overlap in dose or strength

Product name with potential for confusion	Similarity to Asclera	Strength	Recommended Dose
Asclera (Polidocanol)	N/A	Intravenous injection: 0.5% and 1% per 2 mL ampules	0.1 to 0.3 mL of 0.5% per injection for spider veins and 0.1 to 0.3 mL of 1% per injection for reticular veins. Maximum daily dose per treatment (b) (4) (b) (4)
Antara (Fenofibrate)	Look and Sound-alike	Capsule: 43 mg, 87 mg, and 130 mg	Adults: 43 mg-130 mg orally once daily. Elderly: Initially, 43 mg orally once daily. May adjust up to 130 mg once daily.
Aralen (Chloroquine Phosphate)	Look-alike	Tablet: 300 mg (as base)	Adults: The recommended initial dose is 1000 mg (600 mg base) orally, then 500 mg (300 mg base) orally in six to eight hours, then 500 mg (300 mg base) orally once daily for 2 days. Total dose is 2.5 g chloroquine phosphate or 1.5 g base in 3 days. Adults: The FDA-approved prophylactic regimen is 500 mg (300 mg base) orally weekly on the same day of each week, starting two

			weeks before entering the endemic area and continuing for 8 weeks after leaving the area.
Aredia (Pamidronate)	Look-alike	Intravenous: 30 mg, 60 mg, and 90 mg powder for injection	Adult-treatment of hypercalcemia associated with malignancy: 60 to 90 mg given as a single dose, intravenous infusion over at least 2 to 24 hours. To allow time for a full response after the initial dose, wait a minimum of 7 days before retreatment. Adult females- treatment for postmenopausal osteoporosis: Data suggest that 45 mg IV infusion every 3 months, administered as a 15 mg IV infusion over 3 hours once daily for 3 days, or a single 30 mg IV infusion given over 3 hours every 3 months which is not FDA approved.
Ascarel (Pyrantel)	Look and Sound-alike	Oral suspension: 144 mg/mL	Treatment of pinworm-adult, adolescents and children $\geq$ 2 years old and $\geq$ 25 pounds: 11 mg/kg orally as a single dose and dose in two weeks. Maximum dose is 1 gram. Treatment of hookworm- adult, adolescents and children $\geq$ 2 years old and $\geq$ 25 pounds: 11 mg/kg orally once a day for three consecutive days. Treatment of intestinal trichinosis - adult, adolescents and children $\geq$ 2 years old and $\geq$ 25 pounds: 10 mg/kg orally once a day for four consecutive days.
Ceclor (discontinued but generic drugs still marketed) (Cefaclor)	Look-alike	Capsules: 250 mg 500 mg Oral suspension: 125 mg/5 mL 187 mg/5 mL 250 mg/5 mL 375 mg/5 mL	Adult: 250-500 mg every 8 hours not to exceed 1.5 grams/day. Child > 1 month: 20-40 mg/kg/day in divided doses every 8 hours, or total daily dose may be divided and given every 12 hours, not to exceed 1 gram/day

Appendix H: Products with overlap in strength, dose or achievable dose with differentiating product characteristics

Product name with potential for confusion	**Similarity to Asclera**	**Strength**	**Usual Dose (if applicable)**	**Differentiating Product Characteristics (Asclera vs. Product)**
Asclera (Polidocanol)	N/A	Intravenous injection: 0.5% and 1% per 2 mL ampules	0.1 to 0.3 mL of 0.5% per injection for spider veins and 0.1 to 0.3 mL of 1% per injection for reticular veins. Maximum daily dose per treatment day is 0.4 mL/kg body weight for 0.5% solution and 0.2 mL/kg body weight for 1% solution.	N/A
Aclaro (Hydroquinone)	Look-alike	Topical cream 4 %	Adult and children ≥ 12 years old: Apply to the affected area twice daily	Dosage form: Intravenous injection vs. topical Route of administration: local intravenous injection vs. topical Dose: 0.1 to 0.3 mL of 0.5% per injection for spider veins and 0.1 to 0.3 mL of 1% per injection for reticular veins. vs. amount applied to affected area. Frequency: May use up to 16 injections at multiple sites per treatment day in spider veins and up to 8 injections at multiple sites per treatment day in reticular veins (may require repeat treatments for optimal outcome) vs. twice a day. Location of use: Administered by a healthcare professional in a doctor's office or clinic vs. self-administered by patient.
Acular (Ketoralac Tromethamine) Acular LS (Ketoralac Tromethamine)	Look-alike	Ophthalmic: 0.5% preservative free, 0.4% lower strength	Adults, adolescents, and children ≥ 3 years old: One drop into operative eye four times per day up to 4 days post surgery. Cataract surgery: start drops 24 hours postop twice daily up to 14	Dosage form: intravenous injection vs. ophthalmic solution. Route of administration: local intravenous injection vs. topical to eye Dose: 0.1 to 0.3 mL of 0.5% per injection for spider veins and 0.1 to 0.3 mL of 1% per injection for

			days post cataract surgery.	reticular veins vs. One drop into operative eye Frequency: May use up to 16 injections at multiple sites per treatment day in spider veins and up to 8 injections at multiple sites per treatment day in reticular veins (may require repeat treatments for optimal outcome) vs. four times per day up to 4 days post surgery. Cataract surgery: start drops 24 hours postop twice daily up to 14 days post cataract surgery. Location of use: Administered by a healthcare professional in a doctor's office or clinic vs. self-administered by patient.
Aldara (Imiquimod)	Look and Sound-alike	Topical cream: 5%	Adults, Adolescents, and Children ≥ 12 years: Apply a thin layer to the affected areas once daily and cream should be left on the skin for 6-10 hours and then washed off with mild soap and water. Continue therapy until there is a total clearance of warts or for a maximum of 16 weeks	Dosage form: Intravenous injection vs. topical cream Route of administration: local intravenous injection vs. topical Dose: 0.1 to 0.3 mL of 0.5% per injection for spider veins and 0.1 to 0.3 mL of 1% per injection for reticular veins vs. Application of a thin layer Frequency: May use up to 16 injections at multiple sites per treatment day in spider veins and up to 8 injections at multiple sites per treatment day in reticular veins (may require repeat treatments for optimal outcome) vs. 3 times per week (on nonconsecutive nights) just prior to sleep. Location of use: Administered by a healthcare professional in a doctor's office or clinic vs. self-administered by patient.

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21201	ORIG-1	CHEMISCHE FABRIK KREUSSLER AND CO GMBH	AETHOXYSKLEROL (POLIDOCANOL)0.5%/1% 8

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/s/

SHIRLEY A ZEIGLER
12/29/2009

DENISE P TOYER
12/29/2009

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 021201

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Chemische Fabrik Kreussler and Co., GmbH
c/o INC Research, Inc.
650 Peter Jefferson Parkway, Suite 200
Charlottesville, VA 22911

ATTENTION: Howard M. Smith
Assistant Director, Medical Writing

Dear Mr. Smith:

Please refer to your New Drug Application (NDA) resubmission dated July 10, 2009, received July 10, 2009 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Polidocanol Injection 0.5% and 1%.

We also refer to your September 29, 2009, correspondence, received September 30, 2009, requesting review of your proposed proprietary name, Asclera. We have completed our review of the proposed proprietary name, Asclera and have concluded that it is acceptable.

The proposed proprietary name, Asclera, will be re-reviewed if this NDA is not approved on or before the January 10, 2010 goal date. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your September 30, 2009, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Nina Ton, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-1648. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Michael Monteleone at 301-796-1952.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21201	ORIG-1	CHEMISCHE FABRIK KREUSSLER AND CO GMBH	AETHOXYSKLEROL (POLIDOCANOL)0.5%/1% (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/

DENISE P TOYER on behalf of CAROL A HOLQUIST
12/29/2009