CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200045Orig1s000

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 20, 2010
Application Type/Number:	NDA 200045
Through:	Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Kristina A. Toliver, PharmD, Team Leader Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name:	Amturnide (Aliskerin, Amlodipine, and Hydrochlorothiazide) Tablets 150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300mg/5mg/25mg, 300 mg/10 mg/12.5 mg, 300 mg/10 mg/25 mg
Applicant:	Novartis
OSE RCM #:	2010-2232

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

CONTENTS

EXECUTIVE SUMMARY

This review summarizes DMEPA's proprietary name risk assessment of Amturnide (Aliskerin, Amlodipine, and Hydrochlorothiazide) Tablets, 150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300mg/5mg/25mg, 300 mg/10 mg/12.5 mg, and 300 mg/10 mg/25 mg. 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, Amturnide, 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 responds to a November 15, 2010 request from Novartis Pharmaceuticals Corporation for assessment of the proposed proprietary name, Amturnide, regarding potential name confusion with other proprietary or established drug names in the usual practice settings and promotional concerns.

1.2 REGULATORY HISTORY

DMEPA previously evaluated three proposed proprietary names for this NDA. These names are (b) (4) (b) (4) Thus, the name Amturnide has been submitted for our evaluation.

1.3 PRODUCT INFORMATION

Amturnide (Aliskiren, Amlodipine Besylate, and Hydrochlorothiazide) is a combination product which contains a direct renin inhibitor (Aliskiren), a dihydropyridine calcium channel blocker (Amlodipine Besylate), and a thiazide diuretic (Hydrochlorothiazide). This product is indicated for the treatment of hypertension. It is not indicated for initial therapy. Amturnide is dosed once daily and will be available in five strengths: 150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300mg/5mg/25mg, 300 mg/10 mg/12.5 mg, and 300 mg/10 mg/25 mg. Amturnide will be supplied bottles of 30, 90, and unit-dose blister packages of 100.

2 METHODS AND MATERIALS

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

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]

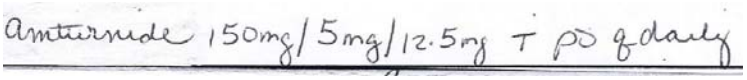
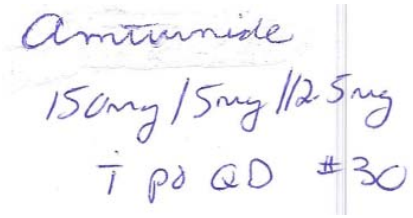
To identify drug names that may look similar to Amturnide, the DMEPA Safety Evaluators also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (9 letters), upstrokes (two, lower case 't' and 'd'), downstrokes (none), cross strokes (one, letter 't'), and dotted letters (one, letter 'i'). Additionally, several letters in Amturnide may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA Safety Evaluators also considers these alternate appearances when identifying drug names that may look similar to Amturnide.

When searching to identify potential names that may sound similar to Amturnide, the DMEPA Safety Evaluators search for names with similar number of syllables (three), stresses (AM-tur-nide, am-TUR-nide, or am-tur-NIDE), and placement of vowel and consonant sounds. Additionally, the DMEPA Safety Evaluators consider that pronunciation of parts of the name can vary (see Appendix B). The Applicant's intended pronunciation of the name was not included in request for proprietary name review.

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. Amturnide Prescription Studies (conducted on November 2, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	Amturnide 150 mg/5 mg/12.5 mg. Take one PO QD.
Outpatient Prescription: 	

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

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

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

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

After the Safety Evaluator has determined the overall risk associated with 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 searches yielded a total of 14 names as having some similarity to the name Amturnide.

Twelve of the 14 names were thought to look like Amturnide. These names are Anturane, Amcinonide, Amantadine, Amnide, Anu-med, Anthralin, Bumetanide, Ciclesonide, Amiloride, Aprezaside, Octreotide, and Amifostine. One name, Antimony, was thought to sound like Amturnide. The remaining name, Amturnide was thought to look and sound similar to Amturnide

Additionally, DMEPA Safety Evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of November 29, 2010.

3.2 CDER EXPERT PANEL DISCUSSION

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

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 25 practitioners responded. Nine of the practitioners interpreted the name correctly as "Amturnide". None of the responses overlapped with any existing or proposed drug names. In the studies, all responses were misspelled variations of the proposed name, Amturnide. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

Med-ERRS did not identify any names which were thought to look or sound alike to Amturnide.

Med-ERRS concluded that Amturnide has a low vulnerability from the safety standpoint.

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

3.5.1 Initial Phase of Review

Due to the short turnaround between the NDA PDUFA and submission of the proposed proprietary name, an email was not sent to the Division at the initial phase of the review.

3.5.2 Midpoint of Review

On November 30, 2010, DMEPA notified DCRP via e-mail that we had no objections to the proposed proprietary name, Amturnide. DCRP stated they "did not have any concerns with the name," Amturnide**.**

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in identification of three additional names, Tekmalo, Tekturna, and Tekturna HCT. These three names, all Novartis products which contain Aliskiren, were evaluated since Amturnide will represent the fourth Novartis product that contains Aliskiren. Additionally, the previously submitted names for the proposed product were found unacceptable (b) (4) . Thus, we evaluated a total of 17 names.

4 DISCUSSION

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.

4.1 PROPRIETARY NAME PROMOTIONAL ASSESSMENT

DDMAC evaluated the name Amturnide from a promotional perspective and determined the name was acceptable. The Division of Cardiovascular and Renal Products and the Division of Medication Error Prevention and Analysis concurred with this assessment.

4.2 PROPRIETARY NAME SAFETY ASSESSMENT

The safety review considered all sources of potential confusion with the proposed name including orthographic and phonetic similarities with currently marketed products.

DMEPA identified and evaluated a total of 17 names for their potential similarity to the proposed name, Amturnide. Nine (n=9) of the 17 names were eliminated from further analysis for the following reasons: five names lacked orthographic and/or phonetic similarity (see Appendix D), one name is the proposed name that is the subject of this review and is trademarked by the Applicant (see Appendix E), two names are not currently marketed products (see Appendix F), and one is unlikely to be written on prescription orders (see Appendix G). Of note, three of the five names eliminated due to lack of orthographic and/or phonetic similarity are Tekamlo, Tekturna, and Tekturna HCT. Thus, the proposed proprietary name, Amturnide, does not have similarity with the currently marketed Aliskiren containing products, Tekamlo, Tekturna, or Tekturna HCT.

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining eight names and, thereby, lead to medication errors. This analysis determined that the name similarity between Amturnide was unlikely to result in medication errors with any of the eight products for the reasons presented in Appendices H and I.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Amturnide, 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, Amturnide, 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 this NDA, 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 re-evaluated. If you have further questions or need clarifications, please contact Brantley Dorch, OSE Project Manager, at 301-796-0150.

5.1 COMMENTS TO THE APPLICANT

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

6 REFERENCES

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

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

2. ***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.

3. ***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.

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)***

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

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

   Provides information regarding patent and trademarks.

9. ***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.

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)***

    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)***

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

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

    List contains all the recognized USAN stems.

14. ***Red Book Pharmacy's Fundamental Reference***

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

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

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

16. ***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 Safety Evaluators 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 Safety Evaluators also conduct 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 Safety Evaluators 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 Safety Evaluators consider 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 Safety Evaluators consider the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[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 Safety Evaluators also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led

---

[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.

to medication errors. The DMEPA Safety Evaluators apply 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 Safety Evaluators compare 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 Safety Evaluators also consider 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 Safety Evaluators conduct 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 Safety Evaluators 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 Safety Evaluators 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) Safety Evaluators 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?"***

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

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

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

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

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 proposed name "Amturnide"	When scripted may appear as:	When spoken may be interpreted as:
Capital 'A'	Cl, Ci, Ce	E
lower case 'm'	m, n, rn	n
lower case 't'	x	d
lower case 'u'	e, v	oo, oh, e
lower case 'r'	n, s	
lower case 'n'	m, r, s	m
lower case 'i'	a, c, e, u	ay
lower case 'd'	cl, ci	t
lower case 'e'	a, c, i, e	ee
Am-	Cim	Em
-tur-	tir, ter, ten, tin	ter, der, dur
-nide	mide, ride	nyde, mide

Appendix C: FDA Prescription Study Responses

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Amiturnide 150 mg/5mg/12.5mg 1 po every day	Amturnide 150 mg/5 mg/12.5 mg; take 1 by mouth daily; dispense 30.	Amtedide 150/5/12.5
Amturide 150 mg/5 mg/12.5 mg one PO daily	Amturnide 150/5 mg /12.5 mg 1 po qd #30	Amteride 150/5/12.5mg
Amturide 150 mg/5mg/122.5mg one by mouth daily	Amturnide 150mg/5mg/12.5mg	Amteride 150mg/5mg/12.5mg
Amturnide 150 mg/5 mg/12.5 mg one po qdaily	Amitrimide 150 mg/5mg/12.5mg 1 po qd #30	Amternide
Amturnide 150mg/ 5mg/ 12.5mg 1 PO QD	Amurnide 150 mg/5 mg/12.5 mg	Amternide 150 mg/5 mg/12.5 mg, 1 tablet once a day, dispense 3
Amturnide 150mg/5mg/12.5mg 1 po daily	Amitranide 150mg/5mg/12.5mg, #30 Take 1 by mouth daily	Amternide 150/5/12.5
Amturnide 150mg/5mg/12.5mg Take 1 by mouth daily	Amturnide 150 mg/5 mg/12.5 mg one PO qday Disp #30	Amternide 150/5/12.5mg, 1 tablet qday
	Amtrumide	Amtronide 150 mg./5 mg./12.5 mg
		Amtronide 150/5/12.5mg, Take 1 tablet once a day. Dispense 3.
		Anternide

Appendix D: Names Lacking Orthographic and/or Phonetic Similarity.

Name	Similarity to Amturnide
Amnide	Look
Anthralin	Look
Tekamlo	Look
Tekturna	Look
Tekturna HCT	Look

Appendix E: Name that is the subject of this review

Name	Similarity to Amturnide
Amturnide	Look and Sound, Trademarked by Novartis

Appendix F: Products no longer marketed with no generic equivalent available

Name	Similarity to Amturnide	Comments
Anturane (Sulfinpyrazone)	Look	Discontinued per Drugs@FDA. *Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**
Apresazide (Hydralazine and Hydrochlorothiazide) Tablets	Look	Discontinued per Clinical Pharmacology and Drugs@FDA, not listed in Red Book

Appendix G: Name unlikely to written on prescription orders

Name	Similarity to Amturnide	Comments
Antimony	Sound	Chemical element

Appendix H: Names with multiple differentiating product characteristics

Product Name	Similarity to Amturnide	Strength	Usual Dose	Other Differentiating Product Characteristics (Product vs. Amturnide)
Amturnide (Aliskiren, Amlodipine. and Hydrochlorothiazide) Tablets		**150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300 mg/5 mg/25 mg, 300 mg/10 mg/12.5 mg, 300 mg/10 mg/25 mg**	**One tablet by mouth once daily**	
Amcinonide Topical Cream and Ointment	Look	0.1%	Apply a thin film to affected area two to three times daily	**Route of administration:** oral vs. topical **Dosage Form:** ophthalmic solution vs. tablet **Dose:** one tablet vs. thin film
Anu-Med (Phenylephrine) Suppositories	Look	0.25%	Insert one suppository rectally up to four times daily	**Route of administration:** oral vs. rectal **Dosage Form:** tablet vs. suppository **Strength:** 150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300 mg/5 mg/25 mg, 300 mg/10 mg/12.5 mg, 300 mg/10 mg/25 mg vs. 0.25% **Dosing Frequency:** once daily vs. up to four times daily
Ciclesonide Available as: Omnaris Nasal Spray Alvesco Inhalation Aerosol	Look	50 mcg/ spray 80 mcg/actuation and 160 mcg/actuation	Nasal Spray: Two sprays in each nostril once daily Inhalation Aerosol: One to two puffs twice daily	**Dosage Form:** tablet vs. nasal spray, inhalation aerosol **Strength:** 150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300 mg/5 mg/25 mg, 300 mg/10 mg/12.5 mg, 300 mg/10 mg/25 mg vs. 50 mcg, 80 mcg, or 160 mcg
Octreotide Injection	Look	50 mcg/mL, 100 mcg/mL, 500 mcg/mL, 100 mcg/mL, 1000 mcg/5 mL	50 mcg to 600 mcg subcutaneously in two to four divided doses daily	**Route of administration:** oral vs. subcutaneous **Dosage Form:** tablet vs. injection **Dose:** one tablet vs. 50 mcg to 600 mcg

Product Name	Similarity to Amturnide	Strength	Usual Dose	Other Differentiating Product Characteristics (Product vs. Amturnide)
Amturnide (Aliskiren, Amlodipine. and Hydrochlorothiazide) Tablets		**150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300 mg/5 mg/25 mg, 300 mg/10 mg/12.5 mg, 300 mg/10 mg/25 mg**	**One tablet by mouth once daily**	
Amifostine For Injection	Look	500 mg	200 mg/m^2 to 910 mg/m^2 intravenously once daily prior to each dose of chemotherapy	**Route of administration:** oral vs. intravenous **Dosage Form:** tablet vs. Injection **Dose :** one tablet vs. 200 mg/m^2 to 910 mg/m^2

Appendix I: Risk of medication errors due to product confusion minimized by dissimilarity of the names or specified product characteristics

Proprietary Name: Amturnide (Aliskiren, Amlodipine, and Hydrochlorothiazide) Tablets	Strength: 150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300 mg/5 mg/25 mg, 300 mg/10 mg/12.5 mg, 300 mg/10 mg/25 mg	Signa: One tablet by mouth once daily
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Amantadine Capsule and Tablet, 100 mg Oral Solution, 50 mg/5 mL *Dose*: 100 mg to 200 mg once daily or in two divided doses	Orthographic similarity: Identical beginning letters (“Am”) Similar length (9 letters vs. 10 letters) Both are available as tablets, and are dose once daily	Medication errors unlikely to occur due to orthographic and product characteristics differences between the names *Rationale:* Amturnide has an upstroke of the letter ‘t’ towards the beginning of the name, and an upstroke of the letter ‘d’ toward the end of the name vs. Amantadine which as upstrokes of the letters ‘t’ and ‘d’ in the middle of the name Amturnide is available in multiple strengths, so the product strength would have to be specified on prescription orders. The strengths of Amturnide do not overlap with the strength of Amantadine.

Proprietary Name: **Amturnide** **(Aliskiren, Amlodipine, and Hydrochlorothiazide) Tablets**	**Strength:** **150 mg/5 mg/12.5 mg,** **300 mg/5 mg/12.5 mg,** **300 mg/5 mg/25 mg,** **300 mg/10 mg/12.5 mg,** **300 mg/10 mg/25 mg**	**Signa:** **One tablet by mouth once daily**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Bumetanide Tablets 0.5 mg, 1 mg, 2 mg Injection 0.25 mg/mL *Dose:* Oral: 0.5 mg to 2 mg by mouth once daily Injection: 0.5 mg to 1 mg intravenously or intramuscularly, repeat 2nd or 3rd dose at two to three hour intervals	Orthographic similarity: Identical ending letters (“nide”) Both are available as tablets, dosed once daily	Medication errors unlikely to occur due to orthographic and product characteristics differences between the names *Rationale:* The beginning letters do not look similar “Amtur” vs. “Bumeta” Amturnide is available in multiple strengths, so the product strength would have to be specified on prescription orders. The strengths of Amturnide do not overlap with the strength of Bumetanide
Amiloride Tablet, 5 mg	Orthographic similarity: Identical beginning letters (“Am”) and ending letters (“ide”) Both are available as tablets, dosed once daily	Medication errors unlikely to occur due to product characteristic differences between the names *Rationale:* Amturnide is available in multiple strengths, so the product strength would have to be specified on prescription orders. Although the 5 mg strength of Amiloride overlaps with the 5 mg strength of Amlodipine in Amturnide, the inclusion of the strengths of the Aliskiren and Hydrochlorothiazide components of Amturnide on prescription orders will differentiate the name pair from one another.

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

/s/

KRISTINA C ARNWINE
12/20/2010

CAROL A HOLQUIST on behalf of DENISE P TOYER
12/21/2010
For Denise Toyer