CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202992Orig1s000

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
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	September 7, 2012
Reviewer:	Jung Lee, RPh Division of Medication Error Prevention and Analysis
Acting Team Leader:	Jamie Wilkins Parker, PharmD Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strengths:	Aubagio (Teriflunomide) Tablets, 7 mg, 14 mg
Application Type/Number:	NDA 202992
Applicant:	Sanofi-aventis
OSE RCM #:	2012-940

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

CONTENTS

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

On August 19, 2011, the Applicant submitted a request for proprietary name review for the proposed proprietary name, Aubagio, under the NDA for this product. The review was completed on November 9, 2011 (OSE RCM # 2011-3129). Aubagio was found to be vulnerable to name confusion that could lead to medication errors with a pending proposed proprietary name, (b) (4) due to orthographic similarity and shared product characteristics. The Applicant was informed in a letter dated November 17, 2011 that the proposed proprietary name was found unacceptable. However, the acceptability of the proposed proprietary name, Aubagio, is dependent upon which application is approved first. DMEPA informed the Applicant, "If Aubagio is approved first, we will advise the second product to seek an alternative name. If the second name application is approved prior to your application then you will be requested to submit another name."

On December 2, 2011, the Applicant submitted a request to review an alternate proprietary name, (b) (4) In their request for the proprietary name review cover letter, the Applicant stated it is their "understanding that should NDA 202992 be approved prior to the other pending application for which the proposed proprietary name may lead to confusion, Aubagio could be used as the proprietary name for teriflunomide regardless of the status of (b) (4)." The name (b) (4) was found to be acceptable on February 29, 2012 (OSE RCM # 2011-4466).

On April 16, 2012, the Applicant withdrew the conditionally acceptable name (b) (4) in order to allow for the re-review of the Applicant's preferred name, Aubagio. The second Request for Proprietary Name Review for Aubagio was submitted on April 16, 2012. The Applicant stated that "should Aubagio be unacceptable after the second review, the sponsor will re-submit (b) (4) for re-review in order to have an acceptable proprietary name at the time of the action date". On April 18, 2012, the PDUFA goal date was extended by three months from June 12, 2012 to September 12, 2012, in order to provide enough time for a full review of the submission due to a major amendment. Subsequently, on June 8, 2012, the Applicant withdrew the Request for Proprietary Name Review for Aubagio with the intention of resubmitting the request within 90 days of the PDUFA goal date for the NDA. On June 11, 2012, the Applicant resubmitted the Request for Proprietary Name Review for Aubagio.

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1.2 PRODUCT INFORMATION

The following product information is provided in the June 13, 2012 (Amendment to Request for Proprietary Name Review) submission.

- Active Ingredient: Teriflunomide
- Indication of Use: For the treatment of patients with relapsing forms of multiple sclerosis (b) (4)
- Route of Administration: Oral
- Dosage Form: Tablet
- Strength: 7 mg, 14 mg
- Dose and Frequency of Administration: One tablet by mouth once daily, with or without food
- How Supplied:
  - Carton of 28 tablets containing 1 wallet composed of 2 folded blister cards of 14 tablets per blister card
  - Carton of 5 tablets containing 1 wallet composed of 1 blister card of 5 tablets
- Storage: Store at 68°F to 77°F (20°C to 25°C) with excursions permitted between 59°F to 86°F (15°C to 30°C)
- Container and Closure Systems: (b) (4) packaged into wallet kits and then into appropriate carton boxes

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Neurology Products concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The May 2, 2012 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

This proprietary name is comprised of a single word that contains the letters "Au" which can be associated with the abbreviation for "both ears". This product is a tablet which is administered orally and not in the ears. In addition, the letters "Au" occur at the beginning of the name which is not the typical placement of the abbreviation on a written prescription; therefore, the likelihood of this abbreviation contributing to a medication error is minimal.

2.2.3 FDA Name Simulation Studies

Thirty-three practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. The majority of the outpatient study participants correctly interpreted the name Aubagio compared to less than half of the inpatient participants and none of the verbal study participants. Of the inpatient participants who misinterpreted the name, all the inpatient participants mistook the letter 'u' in Aubagio for either the letters 'r', 'ra', 'ri', or 'm'. All of the verbal study participants omitted the letter 'u' in the name Aubagio. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, April 19, 2012 e-mail, the Division of Neurology Products (DNP) commented that they thought the name Aubagio was a good choice.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Aubagio. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Aubagio identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines, which were not initially identified and evaluated in OSE Review #2011-3129.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and External Name Study if applicable)

Look Similar		Look Similar		Look Similar	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Antabuse	EPD	(b) (4)	EPD	Entereg	EPD
Aubepine	EPD	Avidoxy	EPD	Natazia	EPD
Auragen	EPD	Avinza	EPD	Qutenza	EPD
Autoject	EPD	Dutoprol	EPD	(b) (4)	EPD

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Our analysis of the 12 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 12 names will not pose a risk for confusion as described in Appendices D and E.

2.2.6 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Neurology Products via e-mail on September 4, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Neurology Products on September 5, 2012, they stated no additional concerns with the proposed proprietary name, Aubagio.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Laurie Kelley, OSE project manager, at 301-796-5068.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Aubagio, and have concluded that it is acceptable. However, if any of the proposed product characteristics as stated in your June 13, 2012 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review.

4 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

   USPTO provides information regarding patent and trademarks.

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

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

9. ***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.

10. ***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.

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

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

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

    USAN Stems List contains all the recognized USAN stems.

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

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

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

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

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

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

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

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

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

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

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

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

19. Dogpile (www.dogpile.com)

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

APPENDICES

Appendix A

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

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

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

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

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

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

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

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

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

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

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

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

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

1. Database and Information Sources

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

2. Expert Panel Discussion

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

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

3. FDA Prescription Simulation Studies

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

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

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

4. Comments from Other Review Disciplines

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

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Aubagio	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'A'	Ce, Cl, D, Fl, H, O, s	Any vowel
Lower case 'a'	el, ci, cl, d, o, u	Any vowel
Lower case 'u'	m, n, r, ri, y, v, w, Any vowel	Any vowel
Lower case 'b'	h, k, l	'p', 'v', 'd'
Lower case 'a'	ci, o, u	Any vowel
Lower case 'g'	j, q, s, y, z	'j', 'z'
Lower case 'i'	c, e, l	Any vowel
Lower case 'o'	a, c, e, u	Any vowel

Appendix C: Prescription Simulation Samples and Results

Figure 1. Aubagio Study (Conducted on April 20, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Aubagio 1 tablet once daily	Aubagio #28 Take one orally daily
Outpatient Prescription: Aubagio #28 Sig: 1 po qd	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Aubagio

As of Date 6/26/2012

84 People Received Study

33 People Responded

Study Name: Aubagio

Total	12	12	9	
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
ABAGEO	0	1	0	1
ABAGGIO	0	1	0	1
ABAGIA	0	2	0	2
ABAGIO	0	6	0	6
ABAJIO	0	1	0	1
ABOGEO	0	1	0	1
AMBAGIO	1	0	2	3
ARABAGIO	1	0	0	1
ARBAGIO	1	0	0	1
ARIBAGIO	5	0	0	5
AUBAGIO	4	0	7	11

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described. (n=7)

No.	Proprietary Name	Active Ingredient	Similarity to Aubagio	Failure preventions
1	Antabuse	Disulfiram	Look Alike	Lacks convincing orthographic similarity
2	Autoject	Injection Device	Look Alike	Lacks convincing orthographic similarity. This is a medical device and not considered a drug.
3	(b) (4)			
4	Avidoxy	Doxycycline (Monohydrate)	Look Alike	Lacks convincing orthographic similarity
5	Avinza	Morphine Sulfate Beads	Look Alike	Lacks convincing orthographic similarity
6	Dutoprol	Metoprolol Tartrate/ Hydrochlorothiazide	Look Alike	Lacks convincing orthographic similarity
7	Entereg	Alvimopan	Look Alike	Lacks convincing orthographic similarity

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Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described. (n=5)

No.	Proposed name: Aubagio Dosage Form: Tablet Strength: 7 mg, 14 mg Usual Dose: One tablet by mouth once daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1	Aubepine (Hawthorn) Dry Extract, Capsule, Tablets, Drops, Syrup, Tea Bags **Strength:** Capsule/Tablet: Various (i.e. 50 mg, 150 mg, 250 mg, 300 mg, 330 mg, 450 mg, 480 mg, 500 mg, 550 mg, 900 mg, etc) Dry Extract, Drops, Syrup, Tea Bags: No strength specified **Usual Dose:** 160 mg to 1800 mg by mouth in 2 to 3 divided doses daily	**Orthographic Similarity:** Both names begin with the letters 'Aub' and contain a downstroke in the 5th position of their names followed by the letter 'i'.	**Orthographic Difference:** Aubepine contains the letter string 'ine' in the suffix which appears different than 'io' in Aubagio when scripted. **Differentiating Product Characteristics:** Dosage Form: Aubepine is available in multiple dosage forms (capsules, tablets, dry extract, drops, syrup, tea bags vs. tablets); therefore, a dosage form would need to be specified when prescribed on an order. Frequency: 2 to 3 times a day vs. once daily

No.	Proposed name: Aubagio Dosage Form: Tablet Strength: 7 mg, 14 mg Usual Dose: One tablet by mouth once daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
2			(b) (4)

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No.	Proposed name: Aubagio Dosage Form: Tablet Strength: 7 mg, 14 mg Usual Dose: One tablet by mouth once daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
3	Auragen (Antipyrine/Benzocaine) Otic Solution **Strength:** 54 mg/mL-14 mg/mL **Usual Dose:** Fill ear canal with 2 to 4 drops; insert saturated cotton pledget. Repeat 3 or 4 times daily, or up to once every 1 to 2 hours	**Orthographic Similarity:** Both names begin with the letters 'Au' and contain a downstroke 'g' in the 5th position of their names.	**Orthographic Difference:** Aubagio contains an upstroke 'b' in the 3rd position which is not seen in Auragen giving the names a different shape and appearance. **Differentiating Product Characteristics:** Strength: Aubagio is available in multiple strengths; thus a strength would need to be specified on the prescription for dispensing. Dose: No dose overlap. Auragen is dosed as 2 to 4 drops vs. Aubagio is dosed as one tablet.
4	Natazia (Estradiol Valerate/Dienogest) Tablets **Strength:** 3 mg/2 mg-2 mg/2 mg-3 mg/1 mg **Usual Dose:** One tablet by mouth once daily	**Orthographic Similarity:** Both names contain 7 letters with a downstroke in the 5th position of their names giving the names a similar shape. **Dosage Form:** Both are tablets. **Dose:** Both can be written as "one" dose without specifying the dosage form (one tablet vs. one tablet). **Frequency:** Both are given once daily.	**Orthographic Difference:** Natazia contains a cross-stroke 't' in the 3rd position which is not seen in Aubagio. In addition, the first letters of the name Natazia, 'Na', does not appear similar to the first letters in Aubagio, 'Au', when scripted. **Differentiating Product Characteristics:** Strength: No strength overlap. Aubagio is available in multiple strengths; thus a strength would need to be specified on the prescription for dispensing.

No.	Proposed name: Aubagio Dosage Form: Tablet Strength: 7 mg, 14 mg Usual Dose: One tablet by mouth once daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
5	Qutenza (Capsaicin) Patch **Strength:** 8% **Usual Dose:** Apply a single, 60-minute application of up to 4 patches. May repeat every 3 months or as warranted by the return of pain.	**Orthographic Similarity:** Both names contain 7 letters, contains the letter 'u' in the 2nd position and a downstroke in the suffix of their names. **Dose:** Both can be written as "one" dose without specifying the dosage form (one patch vs. one tablet).	**Orthographic Difference:** Qutenza contains a cross-stroke 't' in the 3rd position which is not seen in Aubagio. In addition, Qutenza contains 2 letters ('en') before the downstroke 'z' vs. 1 letter ('a') before the downstroke 'g' in Aubagio giving the names a different appearance when scripted. **Differentiating Product Characteristics:** Strength: No strength overlap. Aubagio is available in multiple strengths; thus a strength would need to be specified on the prescription for dispensing. Frequency: 60 minutes vs. once daily

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/s/

JUNG E LEE
09/07/2012

CAROL A HOLQUIST
09/07/2012

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

Proprietary Name Review

Date:	February 29, 2012
Reviewer:	Jung Lee, RPh Division of Medication Error Prevention and Analysis
Team Leader	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	(b) (4) (Teriflunomide) Tablets, 14 mg
Application Type/Number:	NDA 202992
Applicant/Sponsor:	Sanofi-aventis
OSE RCM #:	2011-4466

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JUNG E LEE
02/29/2012

IRENE Z CHAN
02/29/2012

IRENE Z CHAN on behalf of CAROL A HOLQUIST
02/29/2012

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

Proprietary Name Review

Date:	November 9, 2011
Reviewer(s):	Richard A Abate, RPh, MS, Safety Evaluator Division of Medication Prevention and Analysis
Team Leader	Carlos Mena-Grillasca, RPh, Team Leader Division of Medication Prevention and Analysis
Division Director	Carol Holquist, RPh, Director Division of Medication Prevention and Analysis
Drug Name(s) and Strengths:	Aubagio (Teriflunomide) Tablets, 14 mg
Application Type/Number:	NDA 202992
Applicant:	Sanofi
OSE RCM #:	2011-3129

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RICHARD A ABATE
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