# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

**22-425**

# 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**

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|---|---|
| Date: | January 6, 2009 |
| To: | Norman Stockbridge, MD, Director<br>Division of Cardiovascular and Renal Products |
| Thru: | Kellie Taylor, PharmD, MPH, Team Leader<br>Denise Toyer, PharmD, Deputy Director<br>Carol Holquist, RPh, Director<br>Division of Medication Error Prevention and Analysis |
| From: | Jinhee J. Lee, PharmD, Safety Evaluator<br>Division of Medication Error Prevention and Analysis |
| Subject: | Proprietary Name Review |
| Drug Name: | Multaq (Dronedarone HCl) Tablets<br>400 mg |
| Application Type/Number: | NDA # 22-425 |
| Applicant/Applicant: | Sanofi-Aventis U.S. Inc. |
| OSE RCM #: | 2008-1373 |

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## EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Multaq is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) does not object to the use of the proprietary name, Multaq, for this product.

# 1 BACKGROUND

## 1.1 INTRODUCTION

This review was written in response to a request from the Division of Cardiovascular and Renal Products for a final review of the proposed proprietary name, Multaq. Container/Blister labels, blister carton and insert labeling were also provided to be evaluated from a medication errors perspective. Review comments will be provided under a separate cover in a forthcoming review (OSE 2008-1373).

## 1.2 REGULATORY HISTORY

DMEPA previously reviewed the name, Multaq, without objection in ODS Review 05-0075-1, Proprietary Name Review for Multaq (NDA 21-913) dated January 30, 2006.

The Applicant changed the indication and thus, this submission is considered a new NDA.

## 1.3 PRODUCT INFORMATION

Multaq is the proposed name for Dronedarone tablets. Dronedarone is an antiarrhythmic drug with effects from all four classes of the Vaughan Williams' classification. Multaq is proposed to be indicated in patients with a history of, or current atrial fibrillation or atrial flutter, for the reduction of the risk of cardiovascular hospitalization or death. Multaq will be available as 400 mg tablets.

The recommended starting dosage is 400 mg twice daily. Multaq should be taken as one tablet with the morning meal and one tablet with the evening meal.

Treatment with class I or (b) (4) antiarrhythmics (such as flecainide, propafenone, quinidine, disopyramide, dofetilide, sotalol, amiodarone) must be stopped before starting Multaq.

Treatment with Multaq can be initiated in an outpatient setting.

# 2 METHODS AND MATERIALS

This section describes the methods and materials used by the DMEPA staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus of the assessment is to identify and remedy potential sources of medication error prior to drug approval. 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]

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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.

## 2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Multaq, and the proprietary and established names of drug products existing in the marketplace and those pending IND, BLA, NDA, and ANDA products currently under review by CDER.

For the proprietary name, Multaq, the medication error staff of DMEPA search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2).

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 (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.[2] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, the Staff consider the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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 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.[3]

### *2.1.1 Search Criteria*

The medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'M' 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.[4,5]

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

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

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

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

To identify drug names that may look similar to Multaq, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (three, capital letter 'M', 'l', and 't'), downstrokes (one, if "q" is scripted), cross-strokes (one, 't'), and dotted letters (none). Additionally, several letters in Multaq may be vulnerable to ambiguity when scripted, including the letter 'M' may appear as 'N', 'U', or 'V'; lower case 'u' appear as a lower case 'a' or 'o'; and '-taq' may appear as '-tag'. As such, the Staff should also consider these alternate appearances when identifying drug names that may look similar to Multaq.

When searching to identify potential names that may sound similar to Multaq, the Medication Error Staff search for names with similar number of syllables (two), stresses (mul-TAQ or MUL-taq), consonant sound pronunciation ("uhl" versus "ool" or '-tack' versus '-take'), and placement of vowel and consonant sounds. In addition, several letters in Multaq may be subject to misinterpretation when spoken, including the letter 'm' which may be interpreted as 'n' and the letter 'q' may be misinterpreted as 'g'. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Multaq. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the medication error staff were provided with the following information about the proposed product: the proposed proprietary name (Multaq), the established name (Dronedarone HCl), proposed indication (in patients with a history of, or current atrial fibrillation or atrial flutter, for the reduction of the risk of cardiovascular hospitalization or death), strength (400 mg), dose (400 mg or '1 tablet'), frequency of administration (twice daily), route (oral) and dosage form of the product (tablet). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

Lastly, the medication error staff also considers the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

#### 2.1.1.1 Databases and Information Sources

The proposed proprietary name, Multaq, was provided to the DMEPA staff to conduct a search 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 Multaq using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 6.2. To complement the process, the medication error staff 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, the DMEPA staff reviewed the USAN stem list to determine if any USAN stems were present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

#### 2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Multaq. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the DMEPA staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented 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 Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

### *2.1.2 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 Multaq 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 a total of 124 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Multaq 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 prescriptions are optically scanned and one prescription is delivered to a random sample of 124 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 the medication error staff.

**Figure 1. Multaq Study (conducted on September 23, 2008)**

| HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER | VERBAL PRESCRIPTION |
|---|---|
| Inpatient Prescription Order:<br>Multaq 400mg tabs one tabled by mouth w morning and evening meal. | Multaq 400 mg<br>Take 1 tablet by mouth with morning and evening meal. |
| Outpatient Medication Order:<br>Multaq 400mg #60<br>1 tab po with morning an evening meal<br>88 | |

### *2.1.3 Safety Evaluator Risk Assessment of the Proposed Proprietary Name*

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode and Effects Analysis and provide an overall risk 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 name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective then remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking: "Is the name Multaq 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 Multaq 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 and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEPA will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, <u>and</u> demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

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

4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication error staff identifies a potential source of medication error within the proposed proprietary name. 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.

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 is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, JCAHO, and ISMP, have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken 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 the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, 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 limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used 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, and so DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

# 3 RESULTS

## 3.1 PROPRIETARY NAME RISK ASSESSMENT

### *3.1.1 Databases and Information Sources*

The search of the internet and several standard published databases and information sources (see Section 6 References) identified a total of 13 names as having some similarity to the name Multaq.

Ten of the 13 names were thought to look like Multaq, which include: Moxatag,(b) (4) , Multifuge, Multigen, Multihance, Multi-Pak, Mylotarg, and (b) (4) Two names (Multitec and (b) (4) ) were thought to sound like Multaq. One name, Multaq, was thought to look and sound similar to Multaq.

A search of the United States Adopted Name (USAN) stem list on October 31, 2008 identified no USAN stems within the proposed name, Multaq.

### *3.1.2 CDER Expert Panel Discussion*

The Expert Panel reviewed the pool of names identified by the DMEPA staff (see section 3.1.1. above), and commented about the correctness of the dosage form statement, "film-coated tablet".

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

### *3.1.3 FDA Prescription Analysis Studies*

A total of 32 practitioners responded. None of the responses overlap with any existing or proposed drug names. About sixty-nine percent of the participants (n=22) interpreted the name correctly as "Multaq". The misinterpretations occurred in the phonetic prescription study with the prefix in Multaq reported as 'Mo-' instead of 'Mul-'and the suffix reported as '-tac' or '-tak' instead of '-taq'. In the written prescription studies, the suffix was misinterpreted as '-tag'. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

### *3.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name*

Independent searches by the primary Safety Evaluator identified four additional names (Miltuss,(b) (4) and Nal Tab) thought to look similar to Multaq and represent a potential source of drug name confusion. As such, a total of 17 names were analyzed to determine if the drug names could be confused with Multaq and if the drug name confusion would likely result in a medication error.

Four names were not evaluated further because confusion with these names was determined to be unlikely. Multaq was identified as an internationally trademarked name in various databases but does not appear to be marketed in other countries yet. The names,(b) (4) are chemical substances identified in Micromedex, specifically in the Registry of Toxic Effects of Chemical Substances (RTECS) and Dolphin Material Safety Data Sheets, respectively, but was not identified as an active ingredient in any drug product.

The FMEA determined that the name similarity between Multaq and the identified names was unlikely to result in medication errors for the remaining 13 names for reasons outlined in Appendices C through H.

Additionally, because the indication of the product has changed (indicated for rhythm and rate control in patients with atrial fibrillation or atrial flutter, to maintain normal sinus rhythm or to decrease ventricular rate versus in patients with a history of, or current atrial fibrillation or atrial flutter, for reduction of the risk of cardiovascular hospitalization or death), the names (Mylotarg, Mentax, Zantac, Maldec, Ultiva, Multac, and Multi-12) identified in ODS Consult 05-0075-1 (dated January 30, 2006) were reassessed. It was determined that the change in indication did not affect the original risk assessment findings.

## 4 DISCUSSION

### 4.1 PROPRIETARY NAME RISK ASSESSMENT

In this evaluation, DMEPA analyzed 13 names for their similarity to the proposed name Multaq. The findings of the FMEA indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors with any of the names evaluated.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise once the product is commercially marketed. However, DMEPA believes that these limitations are sufficiently minimized by the use of an Expert Panel.

# 5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Multaq, is not vulnerable to name confusion that could lead to medication errors. As such, DMEPA does not object to the use of the proprietary name, Multaq, for this product at this time. However, if **any** of the proposed product characteristics as stated in this review are altered prior to submission of the NDA or approval of the product, DMEPA rescinds this Risk Assessment finding. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

## 5.1 COMMENTS TO THE DIVISION

DMEPA would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any correspondence to the Applicant pertaining to this issue. If you have further questions or need clarifications, please contact Sean Bradley, OSE Project Manager, at 301-796-1332.

## 5.2 COMMENTS TO THE APPLICANT

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

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

If **any** of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

# 6 REFERENCES

## 6.1 REVIEWS

***ODS Review 05-0075-1, Proprietary Name Review for Multaq, Jahng, J. January 30, 2006.***

## 6.2 DATABASES

*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.* ***AMF Decision Support System [DSS]***

DSS is a government database used to track individual submissions and assignments in review divisions.

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

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

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

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

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

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, Rudolphs 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:

The medication error staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The medication error staff 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The medication error staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the medication error staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, DMEPA also considers a variety of pronunciations that could occur in the English language.

**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<br>Identical infix<br>Identical suffix<br>Length of the name<br>Overlapping product characteristics | • Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication<br>• Names may look similar when scripted and lead to drug name confusion in written communication |
| | Orthographic similarity | Similar spelling<br>Length of the name<br>Upstokes<br>Downstrokes<br>Cross-stokes<br>Dotted letters<br>Ambiguity introduced by scripting letters | • Names may look similar when scripted, and lead to drug name confusion in written communication |

| | | | |
|---|---|---|---|
| | | Overlapping product characteristics | |
| Sound-alike | Phonetic similarity | Identical prefix<br>Identical infix<br>Identical suffix<br>Number of syllables<br>Stresses<br>Placement of vowel sounds<br>Placement of consonant sounds<br>Overlapping product characteristics | • Names may sound similar when pronounced and lead to drug name confusion in verbal communication |

**Appendix B**: CDER Prescription Study Responses

| Inpatient Prescription | Voice Prescription | Outpatient Medication Order |
|---|---|---|
| Multaq | Motack | Multaq |
| Multaq | Motac | Multaq |
| Multag | Multaq | Mutaq |
| Multaq | Multac | Multaq |
| Multaq | Multac | Multaq |
| Multaq | Multac | Multaq |
| Multag | | Multaq |
| Multaq | | Multaq |
| Multaq | | Multaq |
| Multaq | | |
| Multaq | | |
| Multaq | | |
| Multag | | |
| Multaq | | |
| Multitag | | |
| Multaq | | |
| Multaq | | |

**Appendix C**: Names that lack convincing orthographic and/or phonetic similarities

| Name | Similarity to Multaq |
|---|---|
| Multifuge | Look |
| Multihance | Look |
| Multi-Pak | Look |

**Appendix D**: Proprietary names used only in Foreign Countries

| Proprietary Name | Similarity to Multaq | Country |
|---|---|---|
| (b) (4) | Look | France – active ingredient is Amino-acid preparation, however, this product is no longer actively marketed. |
| (b) (4) | Look and Sound | Thailand – active ingredient is a multivitamin, however, this product is no longer actively marketed. |
| (b) (4) | Sound | Thailand – active ingredient is a multivitamin and mineral preparation. |

**Appendix E**: Products withdrawn

| Name | Similarity to Multaq | Status |
|---|---|---|
| Multitec | Look and Sound | Application withdrawn by the Commissioner as of January 6, 1989. |
| Nal Tab | Look and Sound | Application withdrawn by the Commissioner as of August 6, 1971. |

**Appendix F**: Products with information not available from the databases listed in the reference section.

| Name | Similarity to Multaq |
|---|---|
| (b) (4) | Sound |

**Appendix G**: Products with no numerical overlap in strength and dose.

| Product name with potential for confusion | Similarity to Multaq | Strength | Usual Dose |
|---|---|---|---|
| **Multaq (Dronedarone HCl)** | | **400 mg** | **Usual dose: 400 mg twice daily.** |
| Moxatag (Amoxicillin) | Look | 775 mg | 775 mg once daily for 10 days with meals. |
| Multigen (Calcium ascorbate, calcium threonate, cyanocobalamin, ferrous asparto Glycinate, Liver stomach concentrate, and succinic acid) | Look | 150 mg/2 mg/10 mcg/70 mg/50 mg/75 mg | Take one tablet daily. |
| Mylotarg (Gemtuzumab ozogamicin) | Look | 5 mg | 9 mg/m$^2$ infused over a 2-hour period. The recommended treatment course with gemtuzumab is a total of 2 doses with 14 days between the doses. Full recovery from hematologic toxicities is not a requirement for administration of the second dose. |

**Appendix H**: Potential confusing name with numerical overlap in dose

| **Multaq (Dronedarone HCl)** | **400 mg** | **Usual dose: 400 mg twice daily.** |
|---|---|---|
| **Failure Mode: Name confusion** | **Causes (could be multiple)** | **Effects** |
| Miltuss (Guaifenesin) | Orthographic similarity - Both names begin with the letter 'M', have identical upstroke and cross stroke letters in similar positions (3rd and 4th), and have a similar number of letters (seven versus six).<br><br>Both have overlapping routes of administration (oral). | Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting.<br><br>*Rationale:*<br><br>When written the names appear similar, however, the presence of a dotted letter, 'i' in Miltuss, and the downstroke letter, 'q', in Multaq, helps to distinguish Miltuss from the proposed name, Multaq. While the strengths and route of administration overlap, the frequency of administration (every 4 hours versus twice daily) and dosage form (oral solution versus tablet) vary. Thus, despite some overlapping product characteristics, we believe the risk for medication error is minimized by the presence of the dotted letter in Miltuss, the downstroke letter in Multaq, as well as the differences in their product characteristics. |

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/s/
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