

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**NDA 22-206**

**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:** June 3, 2008

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Division of Medication Error Prevention (HFD-420)

**Subject:** Division of Medication Error Prevention  
Proprietary Name, Label, and Labeling Review

**Drug Name:** Rapaflo (Silodosin) Capsules  
4 mg and 8 mg

**Application Type/Number:** (IND 56,605)/NDA 22-206

**Applicant:** Watson Pharmaceuticals, Inc.

**OSE RCM #:** 2008-151

\*\*This document contains proprietary drug use data obtained by FDA under contract. The drug use data/information cannot be released to the public/non-FDA personnel without contractor approval obtained through the FDA/CDER Office of Surveillance and Epidemiology.\*\*

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

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## EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Rapaflo, has some similarity to other proprietary drug names, but 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. Thus, the Division of Medication Error Prevention has no objections to the use of the proprietary name, Rapaflo, for this product.

The results of the Label and Labeling Risk Assessment found that the labels and labeling are vulnerable to confusion that could lead to medication errors. We identified areas where information needs to be rearranged or modified in order to make the labels safer to use and less prone to contribute to medication errors. The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMETS rescinds this Risk Assessment finding, and recommends that the name and its associated labels and labeling be resubmitted for review. Additionally, if product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for re-evaluation.

## 1 BACKGROUND

### 1.1 INTRODUCTION

This review was written in response to a request from the Division of Reproductive and Urologic Drug Products (HFD-580) to re-evaluate the proposed proprietary name, Rapaflo, to determine if the name could be potentially confused with other proprietary or established drug names.

### 1.2 REGULATORY HISTORY

This product was originally submitted under IND #56,605 with the proposed proprietary name, Rapaflo. We had no objection to the use of the proposed proprietary name, Rapaflo, in our previous review of the name (OSE Review 2006-0703, dated July 10, 2007). The application is now an NDA (NDA #22-206) and the name has been resubmitted for review and comment.

### 1.3 PRODUCT INFORMATION

Rapaflo (Silodosin) is a highly selective  $\alpha_{1A}$ -adrenoreceptor blocker indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia. The recommended dose is 8 mg once daily with food. However,

the dose should be reduced to 4 mg once daily with food. The 8 mg capsules will be supplied in unit of use bottles containing 30, or 90 capsules and non unit-of-use bottles containing 1000 capsules. The 4 mg capsules will be supplied in unit-of-use bottles containing 30 or 100 capsules. All unit-of-use containers will be supplied with child-resistant closures.

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## 2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the Division of Medication Error Prevention Medication Error Staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and label, labeling, and/or packaging risk assessment (see 2.2 Container, Carton Label, and Insert Labeling Risk Assessment). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention 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.<sup>1</sup>

## 2.1 PROPRIETARY NAME RISK ASSESSMENT

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

For the proprietary name, Rapaflo, the medication error staff of the Division of Medication Error Prevention 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 a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). The Division of Medication Error Prevention normally conducts internal CDER prescription analysis studies and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment. However, since this name was previously evaluated, CDER prescription analysis studies were not conducted upon re-review of Rapaflo.

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 2.1.2). The overall risk assessment is based on the findings of a Failure Modes 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.<sup>2</sup> 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. The Division of Medication Error Prevention 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 considers 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, the Division of Medication Error Prevention 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.<sup>3</sup>

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<sup>1</sup> National Coordinating Council for Medication Error Reporting and Prevention.  
<http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

<sup>2</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

<sup>3</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

### 2.1.1 Search Criteria

The Medication Error Staff consider 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 'R' 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.<sup>4,5</sup>

To identify drug names that may look similar to Rapaflo, 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 (7 letters), upstrokes (3, capital letter 'R', lowercase 'f' and 'l'), downstrokes (2, lowercase 'p' and 'f'), cross-strokes (none), and dotted letters (none). Additionally, several letters in Rapaflo may be vulnerable to ambiguity when scripted, including the letter 'R' may appear as uppercase 'P' or 'K' or lowercase 'n'; lower case 'a' appear as a lowercase 'ce', 'ci', 'e', 'o', or 'u'; lower case 'p' appear as a lower case 'f' or 'g'; lowercase 'f' appear as lowercase 'p' or 't'; lowercase 'l' appear as lowercase 'e', 'b', 'd', or 'o'; lower case 'o' appear as lowercase 'a', 'e', 'l', or 'u'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Rapaflo.

When searching to identify potential names that may sound similar to Rapaflo, the Medication Error Staff search for names with similar number of syllables (three), stresses (RA-pa-flo, ra-PA-flo, or ra-pa-FLO), and placement of vowel and consonant sounds. In addition, several letters in Rapaflo may be subject to interpretation when spoken, including the letters "rapa" which may be interpreted as "rapid"; and the letters "flo" which may be interpreted as "flow". The Sponsor'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 considers 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 (Rapaflo), the established name (Silodosin), proposed indication of use (treatment of the signs and symptoms of benign prostatic hyperplasia), strength (4 mg and 8 mg), dose (4 mg or 8 mg), frequency of administration (once daily), route (oral) and dosage form of the product (capsule). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

Lastly, the Medication Error Staff also consider 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 provide 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, Rapaflo, was provided to the medication error staff of the Division of Medication Error Prevention to conduct a search of the internet, several standard published drug product

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

<sup>5</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Rapaflo using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review the USAN stem list to determine if any USAN stems are 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 the Division of Medication Error Prevention to gather CDER professional opinions on the safety of the product and the proprietary name, Rapaflo. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Error Prevention Medication Errors Prevention 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 Safety Evaluator Risk Assessment of the Proposed Proprietary Name***

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes 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.<sup>6</sup> When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention 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 than 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 Rapaflo 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 Rapaflo to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to

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<sup>6</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

the question is no, the Safety Evaluator is not convinced that the names possess 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.

The Division of Medication Error Prevention will object to the use of proposed proprietary name when 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. The Division of Medication Error Prevention 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, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
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 identify 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 another drug product.

In the event that the Division of Medication Error Prevention objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, the Division of Medication Error Prevention 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 the Division of Medication Error Prevention will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then the Division of Medication Error Prevention will not object to the use of the proprietary name. If any of these conditions are met, then the Division of Medication Error Prevention will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Sponsor/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 Institute of Medicine, World Health Organization, Joint Commission, and Institute for Safe

Medication Practices, 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, the Division of Medication Error Prevention 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 Sponsor, 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 Sponsor'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, we believe 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 (e.g. new form introduced like Lamisil) (see limitations of the process in Section 4).

If the Division of Medication Error Prevention 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. The Division of Medication Error Prevention is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for the Division of Medication Error Prevention 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 we may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

## **2.2 LABEL, LABELING, AND PACKAGING RISK ASSESSMENT**

This section describes the methods and materials used by the Division of Medication Error Prevention medication error staff to conduct a label, labeling, and/or packaging risk assessment (see Section 3 Results). The primary focus of the assessments is to identify and remedy potential sources of medication errors prior to drug approval. The Division of Medication Error Prevention 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.<sup>7</sup>

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container label and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

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<sup>7</sup> National Coordinating Council for Medication Error Reporting and Prevention.  
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.<sup>8</sup>

Because the Division of Medication Error Prevention staff analyzes reported misuse of drugs, the Division of Medication Error Prevention staff is able to use this experience to identify potential errors with all medications similarly packaged, labeled or prescribed. The Division of Medication Error Prevention uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provide recommendations that aim at reducing the risk of medication errors.

The Division of Medication Error Prevention reviewed the following labels and labeling submitted by the Applicant on December 12, 2007. See Appendix J for pictures of the labels.

- Container Labels: 4 mg (30 and 100 count); 8 mg, (5, 30, 90, and 1000 count)
- Blister Pack Sample: 8 mg (3 count)
- Package Insert Labeling (no image)

### 3 RESULTS

#### 3.1 PROPRIETARY NAME RISK ASSESSMENT

##### 3.1.1 Database and Information Sources

The Division of Medication Error Prevention conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Rapaflo to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. Since our previous review, we have identified an additional fifteen names as having some similarity to the name Rapaflo.

Twelve of the fifteen names were thought to look like Rapaflo, which include: \_\_\_\_\_, Replete, Propoflo, Rezulin, Rapadyne, Rapifen, Rapivir, Razadyne, Duraflu, \_\_\_\_\_, and Raptiva. One name, Revatio, was thought to sound like Rapaflo. Two names, Renaflo and Rapport (Rapport Ring Loading System) were thought to look and sound similar to Rapaflo.

Additionally, the Division of Medication Error Prevention did not identify any USAN stems in the name Rapaflo as of March 9, 2008.

##### 3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by the Division of Medication Error Prevention staff (see section 3.1.1. above), and did not note any additional names thought to have orthographic or phonetic similarity to Rapaflo and have the potential for confusion.

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

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<sup>8</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

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**3.1.3 Safety Evaluator Risk Assessment of Proposed Proprietary Name**

Independent searches by the primary Safety Evaluator identified two names, ReFacto and Rapiflux, thought to look and/or sound similar to Rapaflo and represent a potential source of drug name confusion. Thus, from the aforementioned information sources, searches, discussion, and studies, a total of 17 names were analyzed to determine if the drug names could be confused with Rapaflo, and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and/or phonetic similarity to Rapaflo, and thus determined to present some risk for confusion. Failure modes and effects analysis was then applied to determine if the proposed name, Rapaflo, could potentially be confused with any of the 17 names and lead to medication error.

This analysis determined that the name similarity between Rapaflo and the identified names was unlikely to result in medication errors for all 17 products. Six names (Replete, Rapadyne, Razadyne, Rapport, Rapivir, and \_\_\_\_\_) were not considered further because they lack convincing orthographic and/or phonetic similarities to Rapiflo (see Appendix B). One name, Rapifen (Europe, Australia, others) is a foreign drug name for which we could not find product specific information (see Appendix C). Thus, the name was determined by FMEA to pose minimal risk for error in the usual practice setting. Two names, \_\_\_\_\_<sup>\*\*\*</sup>, are pending names within the Agency (see Appendix D). Thus, FMEA determined that these names pose minimal risk for error in the usual practice setting. Propoflo is an injectable veterinary drug product (see Appendix E) and Renaflo (a hemofiltration apparatus) is a non-drug product (see Appendix F); thus, FMEA determined that these names pose minimal risk for error in the usual practice setting. Rezulin is a discontinued product (discontinued in 2003); no generic equivalents are available and thus, this name poses minimal risk for medication errors in the usual practice setting (see Appendix G).

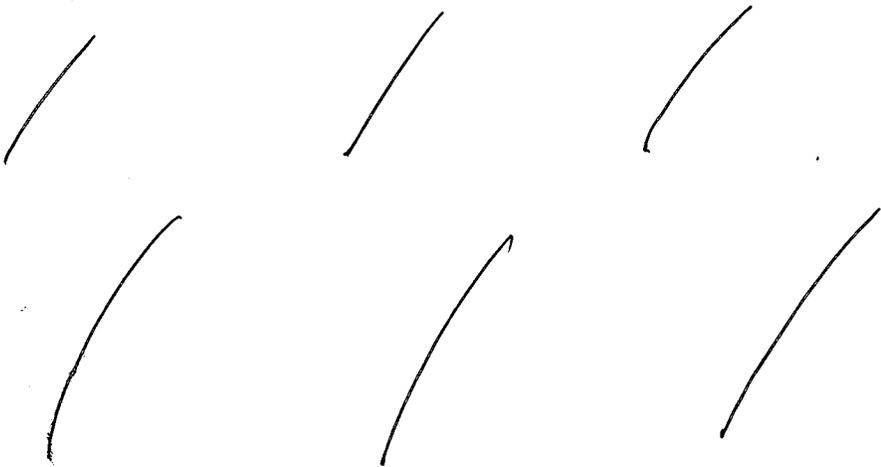
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For three of the names identified (Duraflo, Raptiva, and ReFacto), FMEA determined that medication errors were unlikely because the products do not overlap in strength or dosage with Rapaflo (see Appendix H).

Two names (Revatio, and Rapiflux) had some numerical overlap with Rapaflo in either dosage or strength, but analysis of the failure mode did not determine the effect of this similarity to result in medication errors in the usual practice setting (see Appendix I).

**3.2 LABEL, LABELING, AND PACKAGING RISK ASSESSMENT**

**3.2.1 Container Labels**



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3.2.3 Packaging

The Applicant proposes to market a 5-count bottle of the 8 mg strength capsules.

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3.2.4 Package Insert Labeling

The Division of Medication Error Prevention has no comments.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

The results of the Proprietary Name Risk Assessment found that the proposed name, Rapaflo, has some similarity to other proprietary drug names, but 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.

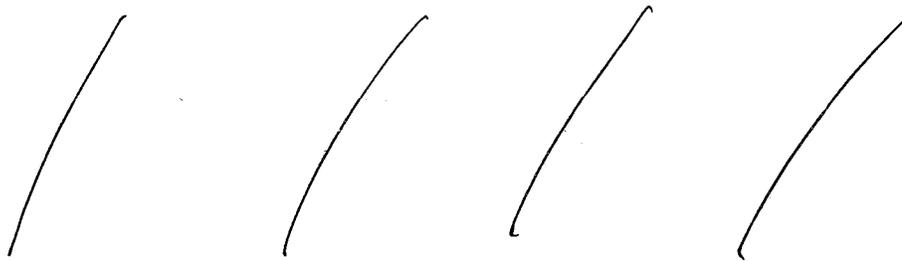
The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves 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. However, the Division of Medication Error Prevention believes that these limitations are sufficiently minimized by the use of an Expert Panel, and the CDER Prescription Studies that involved 123 CDER practitioners.

However, our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, the Division of Medication Error Prevention recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

4.2 LABEL, LABELING, AND PACKAGING RISK ASSESSMENT

[Redacted content]

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## 5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Rapaflo, does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention does not object to the use of the proprietary name, Rapaflo, for this product. Additionally, DDMAC does not object to the proposed name, Rapaflo from a promotional perspective.

Our Label and Labeling Risk Assessment found the \_\_\_\_\_

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\_\_\_\_\_ The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product; the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If 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. Additionally, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

## 6 RECOMMENDATIONS

### 6.1 COMMENTS TO THE DIVISION

We request the revisions outlined below be implemented in the interest of minimizing user errors and maximizing patient safety. The Division of Medication Error Prevention 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 the Division of Medication Error Prevention on any correspondence to the sponsor pertaining to this issue. If you have further questions or need clarifications, please contact Cheryle Milburn, OSE Project Manager, at 301-796-2084.

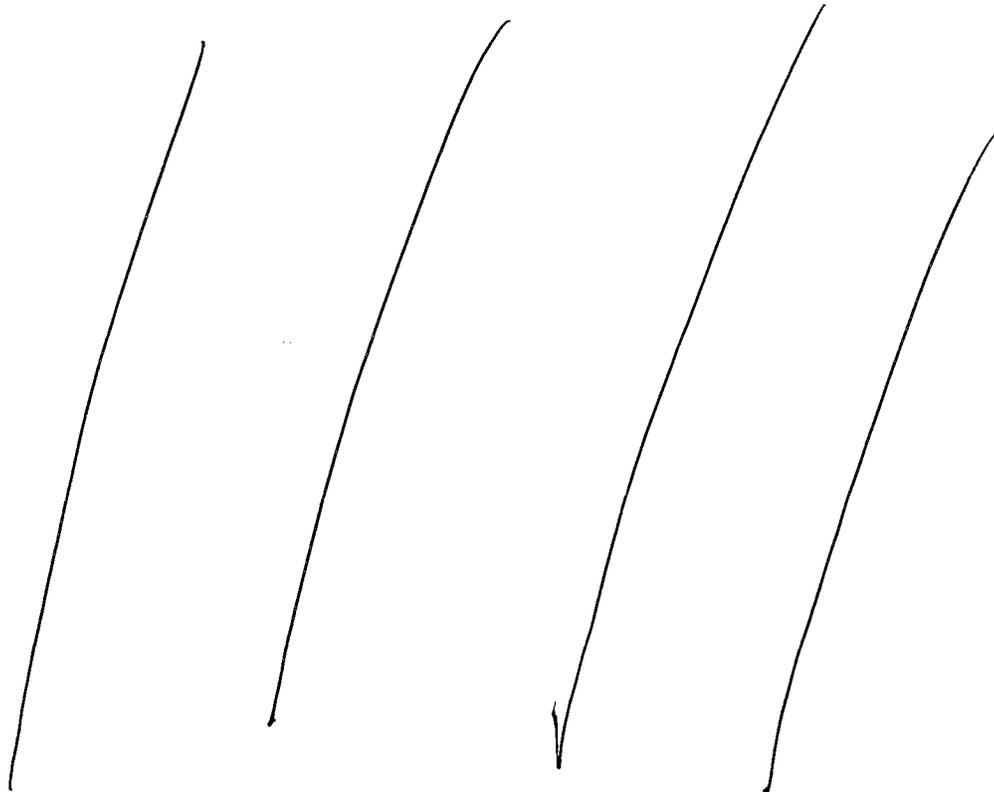
### 6.2 COMMENTS TO THE APPLICANT

#### A. PROPRIETARY NAME

1. The Division of Medication Error Prevention has no objections to the use of the proprietary name Rapaflo for this product.

2. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review.
3. If the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

**B. CONTAINER LABELS**



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**D. PACKAGING**

1. We question the need to market the 8 mg capsule bottle. We have no indication that the

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**E. PACKAGE INSERT LABELING**

1. The Division of Medication Error Prevention has no comments.

**7 REFERENCES**

**1. Adverse Events Reporting System (AERS)**

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have

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

2. ***Micromedex Integrated Index*** (<http://weblern/>)

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

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

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

4. ***Drug Facts and Comparisons, online version, St. Louis, MO*** (<http://weblern/>)

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

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

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

6. ***Division of Medication Errors and Technical Support proprietary name consultation requests***

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

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

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

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

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

9. ***WWW location*** <http://www.uspto.gov>.

Provides information regarding patent and trademarks.

**10. *Clinical Pharmacology Online* (<http://weblern/>)**

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

**11. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)***

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

**12. *Natural Medicines Comprehensive Databases* (<http://weblern/>)**

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

**13. *Stat!Ref* (<http://weblern/>)**

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.

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

List contains all the recognized USAN stems.

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

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

**16. *Lexi-Comp* ([www.pharmacist.com](http://www.pharmacist.com))**

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

**17. *Medical Abbreviations Book***

Contains commonly used medical abbreviations and their definitions.

**18. *Verispan, LLC: Vector One®: National (VONA)***

Verispan's VONA measures retail dispensing of prescriptions or the frequency with which drugs move out of retail pharmacies into the hands of consumers via formal prescriptions. Information on the physician specialty, the patient's age and gender, and estimates for the numbers of patients that are continuing or new to therapy are available.

The Vector One® database integrates prescription activity from a variety of sources including national retail chains, mass merchandisers, mail order pharmacies, pharmacy benefits managers and their data systems, and provider groups. Vector One® receives over 2.0 billion prescription claims per year, representing over 160 million unique patients. Since 2002 Vector One® has captured information on over 8 billion prescriptions representing 200 million unique patients.

Prescriptions are captured from a sample of approximately 59,000 pharmacies throughout the US. The pharmacies in the data base account for nearly all retail pharmacies and represent nearly half of retail prescriptions dispensed nationwide. Verispan receives all prescriptions from approximately one-third of the stores and a significant sample of prescriptions from the remaining stores.

## 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. The Division of Medication Error Prevention 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 led 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 (e.g. "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, the Division of Medication Error Prevention will consider the Sponsor's intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, we also consider 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 Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>

		Downstrokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
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	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

**Appendix B:**

Names that lack convincing orthographic and/or phonetic similarities to Rapaflo

Name	Similarity to Rapaflo
Replete	Look
Rapadyne	Look
Replagal	Look
Razadyne	Look
Rapivir	Look
Rapport	Look and Sound

**Appendix C:**

## Foreign Drug Names

Name	Similarity to Rapaflo	Country
Rapifen	Look	Europe, Australia, and others

**Appendix D:**

## Pending Names Within The Agency

Pending Name	Similarity to Rapaflo
—	Look
—	Look

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**Appendix E:**

## Veterinary Drug Product Name

Name	Similarity to Rapaflo
Propoflo	Look

**Appendix F:**

## Non-Drug Product Names

Name	Similarity to Rapaflo
Renaflo	Look and Sound

**Appendix G:**

## Names of Discontinued Products

Name	Similarity to Rapaflo
Rezulin	Look

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

Product name with potential for confusion	Similarity to Rapaflo	Strength	Usual Dose (if applicable)
Rapaflo (Silodosin)		4 mg and 8 mg	Usual dose: 8 mg once daily with food. _____ _____, the dose is 4 mg once daily with food.
Duraflu	Look	Multiple ingredient tablet: 20 mg/200 mg/60 mg/500 mg	½ or 1 tablet four times per day
Raptiva	Look	Powder for injection: 150 mg (delivers 125 mg/1.25 mL) vials	0.7 mg/kg subcutaneously, initially, then weekly subcutaneous doses of 1 mg/kg (maximum single dose is 200 mg)
ReFacto	Sound	Powder for injection: 200 units, 500 units, and 1,000 units vials	Dosage depends on patient's weight and other factors. Administered intravenously 2 to 3 times per week.

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**Appendix I: Potential confusing name with numerical overlap in strength or dose**

<p><b>Rapaflo</b> (Silodosin)</p>	<p>4 mg and 8 mg</p>	<p>Usual dose: 8 mg once daily with food. <del>_____</del>  <del>_____</del> he dose is 4 mg once daily with food.</p>
<p><b>Failure Mode:</b> Name confusion</p>	<p><b>Causes (could be multiple)</b></p>	<p><b>Effects</b></p>
<p>Razadyne</p>	<p>Orthographic similarity ("Raza")          Potential numerical overlap in strength          (Rapadyne 4 mg/mL oral solution and 8 mg tablets have numbers that overlap with the Rapaflo 4 mg and 8 mg strengths)</p>	<p>Medication error unlikely to occur due to orthographic differences in the names in addition to differing dosing frequencies.</p> <p><i>Rationale:</i>          The risk for medication error is minimized by orthographic differences in the names. Rapadyne has the ending letters "dyne" vs. "flo" in Rapaflo which makes the names look different. Additionally, Razadyne appears longer when scripted because it contains eight letters vs. seven in Rapaflo.</p> <p>Although there is a potential for numerical overlap in the doses of Razadyne and Rapaflo, Razadyne is administered twice daily whereas Rapaflo is administered once daily.</p>
<p>Revatio</p>	<p>Phonetic similarity (Beginning "R" sound and "tio" vs. "flo")          Numerical overlap in dose/strength (20 mg Ravatio dose is achievable with the 4 mg Rapaflo strength)</p>	<p>Phonetic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i>          The risk for medication error is minimized by the phonetic differences in the names. The middle syllable of the names sounds different ("re-VĀ-tio" vs. "RĀ-pa-flo") which helps to differentiate the names.</p> <p>Five 4 mg Rapaflo tablets would be required to make a 20 mg dose if it were mistaken for Ravatio and this may prompt a healthcare professional to double check the prescription.</p> <p>Rapaflo is administered once daily unlike Ravatio which is administered three times per day.</p>
<p>Rapiflux</p>	<p>Orthographic similarity (Entire name "Rapiflo" vs. "Rapiflu")          Phonetic similarity ("Rapi-") and ("-flo" vs. "-flux")</p>	<p>Medication error unlikely to occur due to orthographic and phonetic differences between the names as well as the low number of prescriptions written for Rapiflux.</p> <p><i>Rationale:</i>          The ending letter "x" in Rapiflux helps to differentiate the names. Additionally, the ending syllables ("-flo" vs.</p>

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	Numerical overlap in dose/strength (20 mg Rapiflux dose is achievable with the 4 mg strength of Rapiflo)	“-flux”) sound different. Additionally, based on nationally projected outpatient dispensed prescription data from Verispan, Vector One®: National _____ were dispensed for Rapiflux during the year 2007, and only a total of _____ prescriptions for Rapiflux were dispensed during years 2001 through 2007. <sup>9**</sup>
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<sup>9</sup> Source: Verispan, Vector One®: National, Year 2001 – 2007, Extracted 4-2-08. File: VONA 2008-151 Rapiflux TRx.xls

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