

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

201803Orig1s000

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: October 7, 2010

Application Type/Number: NDA 201803

Through: Zachary Oleszczuk, PharmD, Acting Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Cathy A. Miller, MPH, BSN, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name: Advil ^{(b) (4)} (Sodium Ibuprofen) Tablet
256 mg Sodium Ibuprofen Dihydrate equivalent to 200 mg Ibuprofen

Sponsor: Pfizer Consumer Healthcare

OSE RCM #: 2010-1537

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

INTRODUCTION

This review responds to a July 12, 2010 request from Pfizer Consumer Healthcare for a review of the proposed proprietary names, Advil (b) (4), for safety and promotional concerns with the proposed name.

1.1 PRODUCT INFORMATION

Advil (b) (4) is the proposed proprietary name for Sodium Ibuprofen, 256 mg equivalent to Ibuprofen 200 mg. The recommended dose is one tablet every four to six hours. Advil (b) (4) will be supplied as a 2-count blister, as well as in 20-count, 40-count, 80-count, (b) (4) and 240-count bottles.

DMEPA notes that the Division of Nonprescription Clinical Evaluation is currently under discussion regarding the established name, Sodium Ibuprofen in terms of how the product will be labeled. According to the CMC review, Sodium Ibuprofen is a white crystalline powder that is freely soluble in water. (b) (4) Detailed information for the drug substance is referred to DMF # (b) (4), who submitted an application for a United States Adopted Names (USAN) to the USAN Council on April 4, 2010. Per the CMC review for this application in his initial quality assessment, the drug substance DMF (DMF (b) (4)) needs to be reviewed for fulfillment of CMC requirements and the outcome is currently pending a response from USAN.

2 RESULTS AND DISCUSSION

2.1 REGULATORY CONSIDERATIONS

The Division of Medication Error Prevention and Analysis (DMEPA) seeks input from the Division of Drug Marketing, Advertising, and Communications (DDMAC) during the evaluation of proprietary names for both prescription and OTC products. During the initial steps in the proprietary name review process, DDMAC provided their assessment of the proposed proprietary name, Advil (b) (4) as follows:

DDMAC has been asked to provide input on the proposed over-the-counter (OTC) proprietary name "Advil (b) (4)." We remind you that DDMAC has expertise in prescription drug products, and not in OTC drug products. If the proposed proprietary name was for a prescription drug, we would have promotional concerns because the proposed proprietary name implies superiority over similar products. Specifically, "Advil (b) (4)" contains the word (b) (4) which can be defined as (b) (4)

The drug product's proposed indication is for the temporary relief of minor aches and pains and for the reduction of fever. Therefore, the proposed proprietary name misleadingly implies that the drug offers a clinical improvement over existing therapies by (b) (4) the efficacy of similar products. In the absence of substantial evidence to support the claim that the product provides pain and fever relief beyond that of other products, the proposed proprietary name is misleading.

Please note that the Federal Food Drug and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made, whether through a proposed tradename or otherwise; this includes suggestions the employment of a fanciful proprietary name for a drug or ingredient in such a manner as to imply that the drug or ingredient has some unique effectiveness or composition when, in fact, the drug or ingredient is a common substance, the limitations of which are readily recognized when the drug or ingredient is listed by its established name. [21 CFR 201.10(c)(3)].

2.2 (b) (4) MODIFIER

When reviewing the use of a drug name modifier, DMEPA evaluates a variety of considerations to determine whether the use of the proposed modifier is reasonable and necessary for use with the root name. These considerations include, but are not limited to, whether the drug root name currently exists in the market, and if so, how does the proposed product differ from the root name drug; is there a reasonable rationale provided by the Applicant for the use of the modifier; has the Applicant provided a reasonable definition for the modifier and does that definition align with the rationale for the modifier use; could the proposed modifier potentially cause medication errors; is the modifier currently used in standard nomenclature use for marketed products (i.e. XR=extended-release); and does the modifier exist with different intended meanings?

Additionally, DMEPA performed a search of commonly used drug databases for the use of the modifier (b) (4) in drug names (See Section 6 for a complete listing of commonly used databases). We found a variety of drug names containing the modifier (b) (4). All of the products identified, with the exception of two products (b) (4) are unapproved or monograph products, and therefore, did not undergo the current proprietary name analysis for modifier use that is conducted by DMEPA for prescription and over-the-counter products of all new drug applications. See Appendix A for list of drug names containing the modifier (b) (4). The remaining two of the names, (b) (4) are approved products with names that were approved by the reviewing Divisions of the FDA prior to current guidance procedures in place that require the formal review of proposed proprietary names by the Division of Medication Error Prevention and Analysis.

The Applicant did not specify the intended meaning for the modifier (b) (4). The proposed product contains the active ingredient Sodium Ibuprofen Dihydrate 256 mg, equivalent to Ibuprofen 200 mg. Ibuprofen 200 mg is currently marketed with the proprietary name, Advil. DMEPA believes that the use of the word (b) (4) which can be defined as (b) (4) implies that the active ingredient goes beyond the efficacy of similar products with the same active ingredient even though the proposed active ingredient is equivalent to a common substance (Ibuprofen). DMEPA does not believe that the Applicant's use of the proposed modifier (b) (4) is appropriate for this product pursuant to 21 CFR 201.10(c)(3).

Although there is currently no standardization for the use of drug modifiers (suffixes), the FDA along with the Institutes for Safe Medication Practices (ISMP) has historically recognized the challenges inherent with the inconsistent use of many modifiers. This issue is compounded by the variations in modifier uses for different dosage forms for the same active ingredient. The inconsistent nomenclature used for varying formulations fails to provide cues to patients and practitioners on the proper use for the dosage form or the intended meaning of the modifier.¹ Postmarketing experience has shown that confusion such as this has led to wrong dose and wrong frequency of administration medication errors. ISMP has cited that the error-prone nature inherent to the use of many drug modifiers and that drug marketing considerations impact decisions to use a drug name modifier.²

¹ The Alphabet Soup of Drug Name Suffix, Pharmacy Today, August 2009, page 62.

² ISMP Medication Safety Alert! Volume 9, Issue 3, March 2010.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Advil (b)(4), is unacceptable because it is misleading pursuant to 21 CFR 201.10(c)(3).

DMEPA requested comments from the Division of Nonprescription Clinical Evaluation (DNCE) based on the findings of the misleading nature of the word (b)(4) for the proposed proprietary name, in an email communication dated July 26, 2010. On August 3, 2010, DNCE replied stating that they agree with these findings. Therefore, the Division of Medication Error Prevention and Analysis will not proceed with the safety review of the proposed proprietary name, Advil (b)(4), since the name will be rejected based on misleading concerns. DMEPA will notify the Applicant of FDA's decision to object to the name because of it is misleading.

If you have any questions for DDMAC, please contact Cynthia Collins at 301-796-1200. If you have any further questions or need clarification, please contact Janet Anderson, OSE Project Manager, at 301-796-0675.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of Advil (b)(4), and have concluded that the name is unacceptable for the following reason:

The proposed name 'Advil (b)(4)' is misleading pursuant to 21 CFR 201.10(c)(3) which states:

The employment of a fanciful proprietary name for a drug or ingredient in such a manner as to imply that the drug or ingredient has some unique effectiveness or composition when, in fact the drug or ingredient is a common substance the limitation of which are readily recognized when the drug or ingredient is listed by its established name.

The proposed proprietary name, Advil (b)(4), implies superiority over similar products. Specifically, "Advil (b)(4)" contains the word (b)(4) which can be defined as (b)(4)

(b)(4). The drug product's proposed indication is for the temporary relief of minor aches and pains and for the reduction of fever. Therefore, the proposed proprietary name misleadingly implies that the drug offers a clinical improvement over existing therapies by (b)(4) the efficacy of similar products. In the absence of substantial evidence to support the claim that the product provides pain and fever relief beyond that of other products, the proposed proprietary name is misleading.

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.

4. *Document Archiving, Reporting and Regulatory Tracking System (DAARTS)*

DAARTS 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>)

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDIX

Appendix A: Drug names containing the modifier (b) (4)

PRODUCT NAME	(b) (4)
[Redacted content]	

Appendix A: Drug names containing the modifier (b) (4)

PRODUCT NAME	(b) (4)

Appendix A: Drug names containing the modifier (b) (4)

PRODUCT NAME	(b) (4)
[Redacted content]	

Appendix A: Drug names containing the modifier (b) (4)

PRODUCT NAME	(b) (4)
[Redacted content]	

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

/s/

ZACHARY A OLESZCZUK on behalf of CATHY A MILLER
10/07/2010

ZACHARY A OLESZCZUK
10/07/2010

DENISE P TOYER
10/07/2010

CAROL A HOLQUIST
10/08/2010