CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-106

PROPRIETARY NAME REVIEW(S)

MEMORANDUM	Division of Medication Errors and Technical Support Office of Surveillance and Epidemiology HFD-420; WO22, Mail Stop 4447 Center for Drug Evaluation and Research

To: Janice Soreth, MD
Director, Division of Anti-Infective and Ophthalmology Products

Through: Todd Bridges, RPh, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

From: Diane C. Smith, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

Date: September 27, 2007

Subject: DMETS Proprietary Name Review
Drug: Doribax (Doripenem) Injection
NDA#: 22-106
Sponsor: Johnson & Johnson Pharmaceutical Research & Development, LLC.

Review #: 2007-1924

This memorandum is written in response to a request from the Division of Anti-Infective and Ophthalmology Products for reassessment of the proposed proprietary name, Doribax. DMETS evaluated the proposed name and the associated labels and labeling in OSE review # 2007-465 (dated June 5, 2007). DMETS found the name acceptable at that time and provided label and labeling recommendations to minimize medication errors and in the interest of patient safety.

Since OSE review 2007-465, DMETS has identified five additional names (Clarinex, Duricef, Dynabac, Decabid and Dermabet) as having potential look-alike similarities to Doribax. After evaluation of these five names, DMETS determined that they exhibit minimal potential for confusion for the following reasons:

- Clarinex was not considered further because this name pair lacks convincing look-alike properties as well as having differentiating product characteristics, such as dose (5 mg vs. 500 mg), route of administration (oral vs. intravenous), dosage form (oral tablet and syrup vs. solution for injection), strength (5 mg and 0.5 mg/mL vs. 500 mg) and frequency of administration (once a day vs. every 8 hours).
- Duricef was not considered further because this name pair lacks convincing look-alike properties. Although the product strengths (500 mg) overlap, the frequency of administration (once or twice daily vs. every 8 hours) may help to differentiate these two products when ordered. Additionally, an order for Doribax will likely include the route of administration (intravenous infusion), which will also help to distinguish these names from one another.

- Dermabet was not considered further because Dermabet appears longer than Doribax when scripted. This orthographic difference combined with the differentiating product characteristics such as product strength (0.1% vs. 500 mg) route of administration (topical vs. intravenously) and dosage form (cream vs. solution for injection) will help differentiate these two products when ordered. Additionally, Dermabet is not listed in the 2006 Red Book[1] or at the online drug source, Destination Rx[2].
- Dynabac and Decabid were not considered further because these products have been discontinued and there no generic equivalents available.

In summary, DMETS has no objections to the use of the proposed proprietary name, Doribax. The Division of Drug Marketing and Communication (DDMAC) finds the name, Doribax, acceptable from a promotional perspective. We note that revised labels and labeling were not submitted. Therefore we remind you of our label and labeling recommendations contained in OSE review 2007-465, dated June 5, 2007.

DMETS considers this a final review. However, if the approval of this application is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from the signature of this document. Please copy DMETS on any correspondence to the sponsor pertaining to this review. If you have questions or need clarification, please contact Anne Crandall, OSE Project Manager, at 301-796-2282.

[1] 2006 Red Book, Pharmacy's Fundamental Reference; Thomson.
[2] Web Reference:

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO 22, STOP: 4447)

DATE RECEIVED: February 26, 2007 **DATE OF DOCUMENT:** January 17, 2007	**DESIRED COMPLETION DATE:** April 26, 2007 **PDUFA DATE:** October 12, 2007	**OSE REVIEW #:** 2007-465

TO: Janice Soreth, MD
Director, Division of Anti-Infective and Ophthalmology Products, HFD-520

THROUGH: Linda Kim-Jung, Pharm D, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Walter Fava, R.Ph., Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME: **Doribax** (Doripenem) 500 mg sterile powder **NDA#: 22-106**	**NDA SPONSOR: Johnson & Johnson Pharmaceutical Research & Development, LLC**

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Doribax. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.

2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name, Doribax, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. Please copy DMETS on any correspondence sent to the sponsor pertaining to this review. If you have further questions or need clarifications, please contact Cherye Milburn, Project Manager, at 301-796-2084.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
WO 22, STOP: 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL AND LABELING REVIEW

DATE OF REVIEW: March 13, 2007

NDA#: 22-106 (IND 64,416)

NAME OF DRUG: Doribax
(Doripenem) 500 mg for Injection

NDA HOLDER: Johnson & Johnson Pharmaceutical Research & Development, LLC

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

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anti-Infective and Ophthalmology Products (HFD-520), for assessment of the proprietary name, "Doribax", regarding potential name confusion with other proprietary or established drug names. Package insert labeling along with draft container labels and carton labeling were provided for review and comment.

PRODUCT INFORMATION

Doribax is a carbapenem antibiotic indicated as a single agent for the treatment of intra-abdominal, and complicated urinary tract infections, as well as , pyelonephritis, caused by susceptible strains of microorganisms. It has a broad spectrum of bactericidal activity against gram-positive and gram-negative aerobic and anaerobic bacteria. The recommended dose of Doribax is 500 mg administered every eight hours by intravenous infusion over one hour. It will be available in single use, glass vials containing doripenem powder for constitution with 10 mL of Sterile Water for Injection or 10 mL of 0.9% Normal Saline for Injection.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of the internet, several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Doribax, to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The Saegis[6]

[1] MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, and the electronic online version of the FDA Orange Book.
[4] Phonetic and Orthographic Computer Analysis (POCA)
[5] WWW location http://www.uspto.gov/tmdb/index.html.
[6] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (requisitions) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name. Following completion of these initial components, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a drug must be considered in the overall safety evaluator risk assessment.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Doribax. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proposed proprietary name, Doribax, acceptable from a promotional perspective.

2. The Expert Panel identified eighteen proprietary names that were thought to have the potential for confusion with Doribax. Additionally, an independent review identified two names having look-alike similarities with Doribax.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Doribax 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. These studies employed a total of 124 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Requisition prescriptions were written, each consisting of a combination of marketed and unapproved drug products and included a prescription for Doribax (see page 4). Two different handwritten requisitions were optically scanned as representative samples from the requisitions received, and electronically sent to a random sample of the study participants via electronic mail for their interpretation and review. In addition, the products listed on the requisition were recorded on voice mail, and the voice mail message was sent to a random sample of study participants for their interpretation and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via electronic mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Requisition #1: 2 | 26 | Doribax Requisition #2: 2ic | Doribax 2 vials	Order Code 26 Doribax 2 vials

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Doribax, a total of 20 names were identified as having potential to look and/or sound similar to Doribax. These names are: Durabac, Duradex, Duradex Forte, Doribel, Dovonex, Tobradex, Dostinex, Miralax, Clobex***, Loravex***, Inomax, Doryx, Durabac Forte, Orabase, Dryvax, Darbid, Nuromax, Doriden, Durilux***, and Desilux***.

DMETS also conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Doribax.

Upon analysis of the 20 aforementioned names, 18 names were not reviewed further: Doribel, Dovonex, Tobradex, Dostinex, Miralax, Clobex***, — **, Inomax, Doryx, Durabac Forte, Duradex Forte, Orabase, Dryvax, Darbid, Nuromax, Doriden, — **, and — **. These names were not reviewed further because they lack convincing look-alike/sound-alike similarities with Doribax, in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration and dosage form. Additionally, Darbid, Nuromax, Doriden, were not reviewed further because they are discontinued products and there are no generics available. Furthermore, — *** and — *** were also not reviewed because these two names were withdrawn by the sponsor during the review process.

The remaining two names, Durabac and Duradex, and their product characteristics are discussed in Table 1 (see page 5), along with dosage forms available and usual dose.

Table 1: Potential Sound-Alike/Look-Alike Names for Doribax Identified by DMETS Expert Panel

Product Name	Dosage form(s); Established name	Usual adult dose*	Other**
Doribax	Doripenem sterile powder for injection 500 mg/ 20 mL	500 mg IV every 8 hours infused over one hour	NA
Durabac	Acetaminophen 325 mg, caffeine 50 mg, phenyltoloxamine 20 mg, salicylamide 250 mg Capsule	1 capsule to 2 capsules by mouth every 4 hours not to exceed 8 capsules in 24 hours	LA/SA
Durabac Forte	Acetaminophen 500 mg, caffeine 50 mg, magnesium salicylate 500 mg, phenyltoloxamine 20 mg Extended release tablet	1 tablet by mouth every 4 hours not to exceed 4 tablets in 24 hours	
Duradex	Dextromethorphan 20 mg, Guaifenesin 1200 mg extended release tablet	One tablet by mouth every 12 hours	LA
Duradex Forte	Dextromethorphan 45 mg, Guaifenesin 1200 mg extended release tablet		

*Frequently used, not all-inclusive.
**LA (look-alike) SA (sound-alike)

DMETS has the following comments concerning Durabac and Duradex.

1. Durabac was identified as a name with look-alike and sound-alike similarities to Doribax. Durabac is a prescription combination analgesic product containing acetaminophen 325 mg, caffeine 50 mg, phenyltoloxamine 20 mg, and salicylamide 250 mg. Durabac is also available as Durabac Forte, which contains 500 mg acetaminophen, 50 mg caffeine, 500 mg magnesium salicylate, and 20 mg phenyltoloxamine in an extended release tablet. If a practitioner includes the modifier "Forte" on a prescription, this will differentiate Durabac Forte from Doribax. Thus, DMETS will evaluate the potential for confusion between the root name Durabac and Doribax.

   Orthographic similarities highlighted below show that both names have the letters "d", "r", "b", and "a" in the same sequence of the names. Additionally, both names contain seven letters, making them appear similar in length when scripted.

   Orthographic differences include the appearance of the letters "i" and "x" in Doribax compared to the respective corresponding letters "a" and "c" in Durabac. These differences may help to distinguish the names when scripted.

   Both names contain three syllables which adds to the phonetic similarity between the names. The pronunciation of the first syllable of both names can be almost identical, "dor" vs "dur". Likewise, the letters in the second syllable of both names can also have similar pronunciations "i" vs "a" if the

letter "i" is pronounced like a soft "a". The ending of both names can also have similar pronunciations, especially since the letter "x" in Doribax can sound like the hard letter "c" in Durabac.

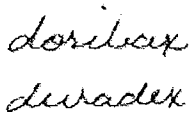
The two names however, do not share any overlapping product characteristics, which may help distinguish the two products. Doribax is an intravenous antibiotic which will be available in a 500 mg strength. Dosage adjustments based on renal function may be required in some patients, therefore physicians would need to include a specific strength when ordering a Doribax infusion for a patient. Additionally, physicians would also need to include frequency and route of administration for each Doribax order. For example, an order for Doribax would read "Doribax 500 mg IV every 8 hours. Infuse over 60 minutes", so that the order would be prepared and administered correctly.

These product characteristics contrast with Durabac which is an oral analagesic containing acetaminophen 325 mg, caffeine 50 mg, phenyltoloxamine 20 mg, and salicylamide 250 mg. Durabac is also available as Durabac Forte which contains acetaminophen 500 mg, caffeine 50 mg, magnesium salicylate 500 mg, and phenytoloxamine 20 mg. Physicians typically may not include a strength when writing medication orders for products with multiple ingredients. However, even if a physician were to write an order as Durabac "500" instead of as Durabac Forte, the route of administration (oral) and frequency of administration (every 4 hours as needed for pain), may minimize the potential for confusion with Doribax. The setting of use may also minimize the potential for confusion between the name pair. Doribax needs to be administered by a healthcare professional in an inpatient, clinic, or home healthcare setting, whereas Durabac is most commonly self-administered on an outpatient basis, although it too can be administered in an inpatient setting.

Despite some orthographic and phonetic similarities between the two names, DMETS believes that the lack of overlapping product characteristics such as frequency and route of administration, will help to minimize the potential for errors to occur between the two products.

2. Duradex was identified as having look-alike similarities to Doribax. Duradex is an extended-release combination product containing guaifenesin 1200 mg and dextromethorphan hydrobromide 20 mg indicated for use in the treatment of upper respiratory tract congestion cough.

   Duradex looks similar to Doribax when scripted because both names have the letters "d", "r", and "x" in the same positions. Moreover, the second letter "d" in Duradex, is an upstroke letter and is located in the same position as the upstroke letter "b" in Doribax. Additionallly, both names also contain seven letters making them appear similar in length when scripted.



The products also do not share any overlapping product characteristics. Doribax is an intravenous antibiotic administered over 60 minutes every eight hours. Dosage adjustments based on renal function may be required in some patients, therefore, physicians ordering Doribax would need to include a strength when ordering a Doribax infusion for a patient. Additionally, physicians would need to include a route of administration (intravenous) and a frequency of administration (every eight

hours) for each Doribax prescription in order for it to be prepared and administered correctly. Prescriptions for Duradex, on the other hand would not necessarily include a strength because physicians may not include strengths on orders for combination products such as Duradex. Duradex is an oral antitussive and expectorant containing guaifenesin 1200 mg and dextromethorphan 20 mg. It is also available as Duradex Forte which contains guaifenesin 1200 mg and dextromethorphan 45 mg. The usual adult dose of Duradex is one tablet by mouth every 12 hours as needed.

The setting of use may also help to minimize confusion between these two products. Doribax will need to be administered in an inpatient, clinic, or home healthcare setting by a healthcare professional, whereas Duradex is primarily self-administered on a outpatient basis.

Despite some look-alike similarities between Doribax and Duradex, the lack of overlapping product characteristics may help to minimize the potential for confusion between Doribax and Duradex.

III. LABELING, PACKAGING AND SAFETY RELATED ISSUES

In the review of the container labels, carton and insert labeling of Doribax, DMETS focused on safety issues relating to possible medication errors. DMETS identified the following areas of possible improvement, which may minimize potential user error.

A. General Comments

1. Copies of the labels and labeling were provided in black and white, therefore DMETS cannot assess if there are any safety concerns due to colors utilized on the labels and labeling. Please submit revised color labels and labeling when available for review and comment.

2. Ensure that the established name on the container label and carton labeling is at least one-half the size of the proprietary name, in accordance with 21 CFR 201.10 (g)(2).

3. Relocate strength to follow established name and revise the strength to read "500 mg/vial" rather than "500 mg doripenem". By expressing the strength in terms of total milligram amount per vial will minimize confusion.

B. Container Labels

1. See General comments A1 through A4.

2. Relocate "Rx only" statement to the bottom portion of primary display panel.

3. If space permits, add statement, "Once reconstituted with 10 mL of Sterile Water for Injection or 0.9% Sodium Chloride for Injection, the resultant concentration is Xmg/X mL".

4. Please standardize the language used in the statement beginning "Each vial contains..." to match the language used on page 9 of the package insert. For example, the statement should read: "Each vial of doripenem monohydrate contains 500 mg doripenem on an anhydrous basis".

5. The statement "Single-use vial" on the primary display panel and side panel should include a

6. The statement "FOR INTRAVENOUS INFUSION", should not be in all capital letters, because it is difficult to read.

C. Carton Labels

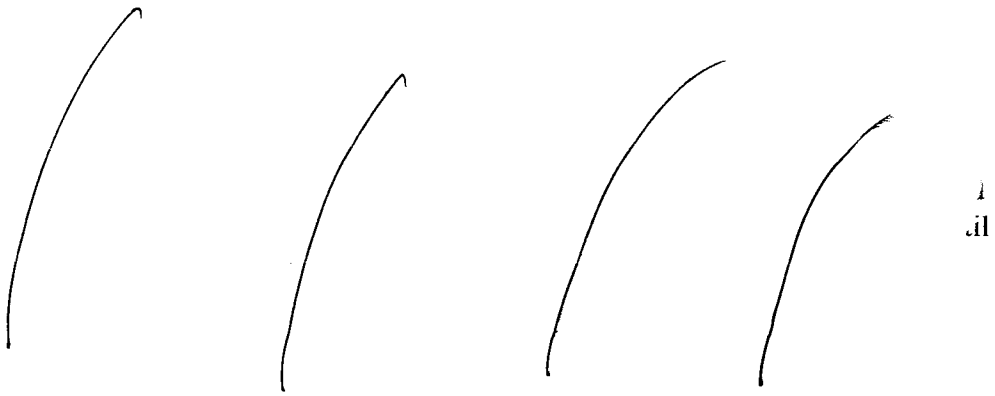
1. See General comments A1 through A4.

2. See Comments B3 and B4.

D. PACKAGE INSERT LABELING

1. See General Comments A1 through A3.

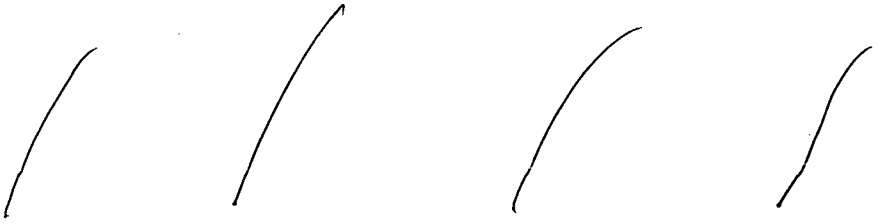
2. Section 2.4, "Preparation of Solutions" should be



3. Section 2.6, "Storage of Constituted Solutions"

a. Change title of Table read "Storage and Stability of Infusion Solutions Prepared in Normal Saline or 5% Dextrose".

b. Clarify Table 2 to clearly show the maximum product stability after dilution, so that no explanatory footnote is required to understand the data.



4. Section 3, "Dosage Forms and Strengths"

a. Delete " — ," from the sentence reading "Single use clear — glass vials...", because it is confusing.

5. Section 16, "How Supplied/Storage and Handling"

   a. Delete the statement:
   since the vial will contain a lot number and expiration date.

Requisition #1	Requisition #2	Verbal
Doribax	Duibax	Dorovax
Deribax 2 vials	Duibax	Durabax 2 vials
Duibax	Direbax	Doravax 2 vials
Deribax	Duibax	Dorabax
Deribax	Duibax	Durabax
Deribax	Duibax	Doravax
Doribax	Duibax	Doravac
Deribax	Dribax	Dorvax
Doribax	Duibax	Dorabax
Deribax	Duibax	Dorabax
Deribax	Duibax	Dorabax
Deribax		Doravax
Deribax		Dorobacks
Doribax		

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/s/

Walter Fava
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Linda Kim-Jung
6/4/2007 01:56:30 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
6/5/2007 10:31:24 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
6/5/2007 10:44:30 AM
DRUG SAFETY OFFICE REVIEWER