CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-110

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:	August 7, 2009
To:	Wiley Chambers, MD, Acting Director Division of Anti-Infective and Ophthalmology Products
Through:	Denise Toyer, Pharm.D., Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Kristina C. Arnwine, PharmD, Team Leader Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Vibativ (Telavancin) for Injection, 250 mg and 750 mg
Application Type/Number:	NDA 22-110
Applicant/Applicant:	Theravance, Inc.
OSE RCM #:	2009-644

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

CONTENTS

1 EXECUTIVE SUMMARY

The re-assessment of this proprietary name is written in response to a notification that a regulatory action on NDA 22-110 may occur within 90 days. DMEPA found the proposed proprietary name, Vibativ, acceptable in OSE Review #2008-1397 on November 26, 2008.

Our safety review focused on new names that have been approved or submitted since our last review and any changes in the proposed product characteristics of Vibativ that may have lead to name confusion. Since our last review, none of Vibativ's product characteristics have been altered.

During this re-review we identified thirteen new names for their similarity to Vibativ. Additionally, on April 23, 2009, DDMAC reviewed the proposed name and had no concerns regarding the proposed name from a promotional perspective and did not offer any additional comments relating to the proposed name

The results of the Failure Mode Effects Analysis found that the proposed name, Vibativ, is not vulnerable to name confusion that could lead to medication errors with any of the 13 names. Thus, the Division of Medication Error Prevention and Analysis finds the proprietary name, Vibativ, acceptable for this product.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Psychiatry Products should notify DMEPA because the proprietary name must be re-reviewed prior to the anticipated action date.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a re-assessment of a proprietary name 90 days prior to approval of an application. Section 2.1 identifies the specific search criteria associated with the proposed proprietary name, Vibativ.

2.1 SEARCH CRITERIA

We used the same search criteria used in OSE Review# 2008-1397. Please refer to Section 2.1.1 of that review for the search criteria.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches of the databases referred to in Section 6 yielded a total of 18 names as having some similarity to the name Vibativ. Fourteen names were thought to look similar to Vibativ. Those names were Ultiva, Rebotin, Ribotin, Vibeden, Vibelan, Vibazine, Vibovit-C, Vivarin, Natalins, ( ) ( ), Librium, Ribatab, and Vectibix. The four remaining names, Viactiv, Vivactil, Vibra-Tabs, and Vivotif were thought to look and sound similar to Vibativ. None of the names were thought to sound like Vibativ. b(4)

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 31, 2009.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel, as described in Appendix A, section 2, reviewed the pool of names identified by DMEPA staff (See Section 2.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Vibativ.

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

3.3 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in no additional names which were thought to look or sound similar to Vibativ and represent a potential source of drug name confusion.

Five of the 18 names (See Appendix B) were identified in the previous Vibativ proprietary name review. None of Vibativ's product characteristics have changed since the previous review. Therefore, the original assessment is maintained. Please see OSE# 2008-1397 for a detailed analysis of these names. As such, 13 new names were analyzed to determine if the drug names could be confused with Vibativ.

4 DISCUSSION

DDMAC had no concerns with the name. The product characteristics have not been altered since our last review. Therefore previously reviewed names were not re-evaluated. Since the previous review, 13 new names were identified and evaluated for their potential similarity to the proposed name, Vibativ. Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the names and lead to medication errors. This analysis determined that the name similarity between Vibativ was unlikely to result in medication errors with any of the thirteen products for the reasons presented in Appendices B through H.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Vibativ, is not vulnerable to name confusion that could lead to medication errors nor is it promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Vibativ, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Anti-Infective and Ophthalmology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Darrell Jenkins, OSE Project Manager, at 301-796-0558.

6 REFERENCES

1. ***OSE 2008-1397, DMEPA Proprietary Name Review***

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

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

3. ***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.

4. ***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.

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 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.

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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

8. ***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.

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

USPTO provides information regarding patent and trademarks.

10. ***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.

11. ***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.

12. ***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.

13. ***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.

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

USAN Stems List contains all the recognized USAN stems.

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

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

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

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

17. ***Medical Abbreviations Book***

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

APPENDICES

Appendix A:

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

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name.

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. DMEPA bases

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

the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors..

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff 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] DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines 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 even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies 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). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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

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

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

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

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

1. Database and Information Sources

DMEPA staff conducts searches 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 the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA 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 DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff 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 primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[4] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?"***

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

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

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

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

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

the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

a. 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 PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

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

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

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

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

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA 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. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, 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 approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to

receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

Appendix B: **Names previously reviewed determined not to pose a safety risk**

Proprietary Name	Similarity to Vibativ
Viactiv	Look-Alike and Sound-Alike
Vivactil	Look-Alike and Sound-Alike
Ultiva	Look-Alike
Vibra-Tabs	Look-Alike and Sound-Alike
Vivotif	Look-Alike and Sound-Alike

Appendix C: **Drug products that are discontinued and no generic equivalent is available**

Proprietary Name	Similarity to Vibativ	Status and Date
Vibazine (Buclizine Hydrochloride)	Look-Alike	Withdrawn by the commission September 22, 1999

Appendix D: **Proprietary or Established Names used only in Foreign Countries**

Proprietary Name	Similarity to Vibativ	Country
Rebotin	Look-Alike	India
Ribotin	Look-Alike	South Korea
Vibeden	Look-Alike	Denmark
Vibelan	Look-Alike	Canada
Vibovit-C	Look-Alike	Poland

Appendix E: **Product names not found in commonly referenced databases (See Section 6, References 1 through 16)**

Name	Similarity to Vibativ
( )	Look

b(4)

Appendix F: **Products with no numerical overlap in strength, dose and route of administration**

Product name with potential for confusion	Similarity to Vibativ	Strength	Usual Dose
Vibativ (Telavancin) for Injection		250 mg and 750 mg	10 mg/kg over 1 hour by intravenous infusion once daily for 7 to 14 days. Dose adjustment for renal impairment to 7.5 mg/kg.
Natalins	Look-Alike	Riboflavin - 1.6 mg Niacin - 17 mg Iron - 60 mg Copper - 3 mg Biotin - 0.03 mg Calcium - 200 mg Folic Acid - 1 mg Magnesium – 100 mg Pantothenic Acid - 7 mg Thiamine - 1.5 mg Cyanocobalamin - 2.5 mcg Ascorbic Acid - 80 mg Pyridoxine - 4 mg Zinc - 25 mg Vitamin E - 15 International Units Vitamin D - 400 International Units Vitamin A - 4000 International Units	One tablet by mouth daily
( ) ( )	Look-Alike	Ascorbic Acid - 60 mg Thiamine - 1.7 mg Riboflavin - 2 mg Pyridoxine - 4 mg Cyanocobalamin - 8 mcg Vitamin A - 5000 International Units Vitamin D - 400 International Units Vitamin E - 30 International Units Folic Acid - 800 mcg Niacinamide - 20 mg Calcium – 200 mg Iodine - 150 mcg Iron (FERROUS FUMARATE) - 60 mg Magnesium - 100 mg Zinc - 15 mg Copper - 2 mg	One tablet by mouth daily.

b(4)

Appendix G: Products with overlap in strength, dose or achievable dose with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Vibativ	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics
Vibativ (Telavancin) for Injection		**250 mg and 750 mg**	**10 mg/ kg over 1 hour by intravenous infusion once daily for 7 to 14 days. Dose adjustment for renal impairment**	
Ribatab (Ribavirin) Tablets	Look-Alike	Oral: 200 mg, 400 mg Oral Solution: 40 mg/ mL	400 mg to 600 mg by mouth twice daily	**Dosage form:** for injection vs. tablets **Route of administration:** intravenous vs. oral **Dosing frequency:** once daily vs. twice daily
Vivarin (Caffeine) tablet	Look-Alike	200 mg	100 mg to 200 mg orally every 3 to 4 hours	**Dosage form:** for injection vs. tablets **Route of administration:** intravenous vs. oral **Dosing frequency:** once daily vs. every 3 to 4 hours

Appendix H: Potential confusing name with numerical similarity in strength or dose

Proprietary Name **Vibativ**	**Strength** **250 mg and 750 mg**	**Usual Dose: 10 mg/ kg over 1 hour by intravenous infusion once daily for 7 to 14 days. Dose adjustment for renal impairment to 7.5 mg/kg**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Vectibix (Panitumumab) injection 20 mg/mL (5 mL,10 mL, 20 mL) 6 mg/kg intravenoulsly every 2 weeks	Orthographic similarities: Similar beginnings (Vi- vs. Ve-) and similar endings (-tiv vs. -bix) Potential numeric overlap in dose since both products are weight-based and the per kilogram doses are close in value (10 mg/kg vs. 6 mg/kg) Overlap in dosing frequency (two weeks)	Orthographic differences between the names and differing product characteristics minimize the likelihood of medication error in the usual practice setting. *Rationale:* Vibativ differs orthographically from Vectibix as there are two letters before the upstroke in Vibativ (Vi-) vs. three letters before the upstroke in Vectibix (Vec-) which make Vectibix appear longer. Addtionally,, although Vibativ and Vectibix contain the same upstrokes ('b' and 't'), they are in the opposite position in each name ('b' then 't' in Vibativ vs. 't' then 'b' in Vectibix.
Librium :hlordiazepoxide) Capsules: 5 mg, 10 mg, 25 mg for Injection: 100 mg	Orthographic similarities: Similar beginnings (Vib- vs. Lib-) Numeric similarities in strength: 250 mg vs. 25 mg Potential overlap in dose: 100 mg to 300 mg	Orthographic differences between the names and differing product characteristics minimize the likelihood of medication error in the usual practice setting. *Rationale:* Vibativ differs orthographically from Librum as Vibativ has an upstroke ('t') in the end of the name, unlike Librium which does not. T Although there is a potential overlap in dose, however a dose of 100 mg to 300 mg of Vibativ would be for children weighing 10 kg to 30 kg respectively. The use of Vibativ in children has not been studied. Additionally, the drugs differ with regard to dosing frequency (once daily for 7 to 14 days vs. three to four times daily).

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/s/

KRISTINA C ARNWINE
08/07/2009

DENISE P TOYER
08/07/2009

CAROL A HOLQUIST
08/07/2009

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:	November 26, 2008
To:	Wiley Chambers, MD, Acting Director Division of Anti-Infective and Ophthalmology Products
Thru:	Kristina C. Arnwine, PharmD, Acting Team Leader Denise P. Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (HFD-420)
From:	Tselaine Jones Smith, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (HFD-420)
Subject:	Proprietary Name Review
Drug Name(s):	Vibativ (Telavancin for Injection) 250 mg and 750 mg
Application Type/Number:	NDA #22-110
Applicant/sponsor:	Theravance, Inc
OSE RCM #:	2008-1397

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

Contents

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Vibativ, is not vunerable to name confusion that could lead to medication error. Thus, DMEPA has no objections to the use of the proprietary name, Vibativ. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, if the product is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

1.1 INTRODUCTION

This re-review for the proposed name, Vibativ, was written in order to rule out any objections to the proposed proprietary name based upon approval of other proprietary or established names from the signature date of the previous Division of Medication Error Prevention and Analysis.

The Applicant did not submit updated labels and labeling for review at this time.

1.2 REGULATORY HISTORY

The Division of Medication Error Prevention and Analysis' initial review of the proposed name (OSE Review # 2007-964 dated August 3, 2007) objected to the name based on concerns of orthographic similarity between Vibativ and Rifadin. Additionally, DMEPA provided label and labeling recommendations in that review.

Subsequently, on September 14, 2007, the Sponsor submitted a rebuttal letter regarding our objection to the name Vibativ. The Division of Medication Error Prevention and Analysis (OSE # 2007-2037) reversed our decision on the acceptability of the name and agreed with the sponsor that there was minimal risk for confusion between Vibativ and Rifadin based on the decreased use of Rifampin and the increased likelihood that when it is prescribed, practitioners will most likely use the established name rather than the Rifadin brand name; thereby, finding the use of the name Vibativ acceptable.

1.3 PRODUCT INFORMATION

Vibativ, Telavancin for injection, is a lipoglycopeptide antibiotic indicated in patients with complicated skin and skin structure infections (cSSI) caused by susceptible strains of the following gram-positive microorganisms: *Staphylococcus aureus* (MRSA and MSSA), *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosis* group, and *Enterococcus faecalis.*

The recommended dosing for Vibativ is 10 mg/kg administered over a 60 minute period by intravenous infusion once every 24 hours for 7 to 14 days. Dosage adjustment for patients with moderate or severe renal impairment is as follows: Creatinine clearance of >50 mL/min: 10 mg/kg every 24 hours, 30-50 mL/min: 7.5 mg/kg every 24 hours, and <30 mL/min [redacted] 10 mg/kg every 48 hours. b(4)

Vibativ requires reconstitution and further dilution prior to administration. The reconstitution is done with 15 mL of 5% Dextrose Injection, USP; Sterile Water for Injection, USP, or 0.9% Sodium Chloride Injection, USP, to achieve an initial concentration of 15 mg/mL. The reconstituted Vibativ solution must be further diluted into 100 mL to 250 mL of the appropriate solution to a final dosing concentration of 0.6 mg to 8 mg/mL. Appropriate infusion solutions include: 5% Dextrose Injection, USP; 0.9% Sodium Chloride Injection, USP; or Lactated Ringer's Injection, USP.

The reconstituted medication is stable as long as the total time in the vial plus the time in the intravenous bag does not exceed [redacted] hours at room temperature and 72 hours under refrigeration. b(4)

Vibativ may be administered intravenously through a dedicated line or through a Y-site. Other intravenous substances, additives, or medications should not be added to Vibativ single-use vials or infused simultaneously through the same intravenous line. If the line is to be used for infusing other medications, the line should be flushed before and after infusion of Vibativ with 5% Dextrose Injection, USP; 0.9% Sodium Chloride Injection, USP; or Lactated Ringer's Injection, USP.

2 METHODS AND MATERIALS

This section describes the methods and materials used by DMEPA medication error staff conducting a proprietary name risk assessment (see section 2.1). The primary focus for both of the assessments 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]

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Vibativ, 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, Vibativ, the medication error staff of DMEPA searched 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 Division of Medication Error Prevention and Analysis normally conducts internal FDA 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, FDA prescription analysis studies were not conducted upon re-review of the proprietary name Vibativ.

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 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. [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 lead to medication errors in the clinical setting. The Division of Medication Error Prevention and Analysis 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. [3] 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,

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

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

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, 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.[4]

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 'V' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter[5, 6]

To identify drug names that may look similar to Vibativ, 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 (three, capital letter 'V', lower case letters 'b' and 't'), downstrokes (none), cross-strokes (one, lower case letter 't'), and dotted letters (two, lower case 'i'). Additionally, several letters in Vibativ may be vulnerable to ambiguity when scripted, including the letter 'V' may appear as lower case 'r' and upper case letter 'L'; lower case 'b' appears as lower case 'h' or 'la'; and lower case 't' may appear as lower case letters 'f' or 'l'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Vibativ.

When searching to identify potential names that may sound similar to Vibativ, the Medication Error Staff search for names with similar number of syllables (3), stresses (VI-ba-tiv, vi-BA-tiv or vi-ba-TIV), and placement of vowel and consonant sounds. In addition, several letters of Vibativ may be subject to interpretation when spoken including the letter 'V' which may be interpreted as the letter 'B', the letter 't' may be interpreted as the letter 'd' and the letters '-iv-' which may be interpreted as '-ic-'. The Applicants 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 (Vibativ) the established name (telavancin), proposed indication (treatment of complicated skin and skin structure infections), strength (250 mg and 750 mg), dose (10 mg/kg administered over a 60 minute period), frequency of administration (once daily for 7 days to 14 days), route of administration (intravenous) and dosage form of the product (lyophilized powder for injection). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff generally take into consideration.

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

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 look and sound-alike 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.

2.1.2 Database and Information Sources

The proposed proprietary name, Vibativ, was provided to the medication error staff of DMEPA 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 Vibativ 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.

2.1.3 CDER Expert Panel Discussion

An Expert Panel Discussion was held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Vibativ. Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. This group is composed of DMEPA 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.

2.1.4 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 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.[5] 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

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

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 Vibativ 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 Vibativ 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, 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 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 Sponsor; 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, all who 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 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, 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 Sponsor 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 Sponsor 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 Database and Information Sources

Searches identified twenty five names as having some similarity to the name Vibativ.

Twenty of the twenty-five names were thought to look like Vibativ, which include: Viaflex, ( ):***, Vibolex, Vibelve, Zorbtive, Vivactil, Librium, Vibratabs, Relafen, Zebeta, Rebetol, Relistor, Reloxin***, Vitafol, Vibeden, Vibeline, Vibazine, Vibion, Vibhitaki and Vibalt. Four of the twenty-five names were thought to look and sound like Vibativ, which include Vivotif Berna, Vibovit, Vigabatrin and Vibovit C. The remaining name, Vibetrat was thought to sound similar to Vibativ. b(4)

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (see section 3.1 above), and noted no additional names.

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 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator identified no additional names thought to look or sound similar to Vibativ and represent a potential source of drug name confusion.

As such, a total of 25 names were analyzed to determine if the drug names could be confused with Vibativ, and if the drug name confusion would likely result in a medication error.

Failure modes and effects analysis was then applied to determine if the proposed name, Vibativ, could potentially be confused with any of the 25 names and lead to medication errors. This analysis determined that the name similarity between Vibativ and the identified names was unlikely to result in medication errors for all 25 products for reasons described/outlined in Appendices B through I.

4 DISCUSSION

We evaluated a total of 25 names for their potential confusion with Vibativ. Our FMEA found 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 once the product is commercially marketed. However, DMEPA believes that these limitations are sufficiently minimized by the use of an Expert Panel.

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, DMEPA recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

5 CONCLUSIONS

The results of the Proprietary Name Risk Assessment found that the proposed name, Vibativ, is not vunerable to name confusion that could lead to medication error. Thus, DMEPA has no objections to the use of the proprietary name, Vibativ. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and the proposed name must be resubmitted for review. 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

The Division of Medication Error Prevention and Analysis would appreciate feedback of the final outcome of this review. We will be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any correspondence to the applicant pertaining to these issues. If you have further questions or need clarification, please contact Darrell Jenkins, OSE Project Manager, at 301-796-0558.

6.2 COMMENTS TO THE APPLICANT

6.2.1 Proprietary Name

The Division of Medication Error Prevention and Analysis has no objection to the use of the proprietary name, Vibativ. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and the proposed name must be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

7 REFERENCES

1. Review of Safety Applications

OSE Review # 2007-964, August 3, 2007 (Vibativ Proprietary Name Review)

OSE Review # 2007-2037, October 19, 2007 (Vibativ Proprietary Name Review)

2. 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.

3. Micromedex Integrated Index (http://weblern/)

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

4. 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 DMEDP, FDA.

5. 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.

6. AMF Decision Support System [DSS]

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

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

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

8. 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.

9. 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.

10. WWW location http://www.uspto.gov.

Provides information regarding patent and trademarks.

11. 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.

12. 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 tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

13. 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.

14. 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, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

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

List contains all the recognized USAN stems.

16. Red Book Pharmacy's Fundamental Reference

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

17. Lexi-Comp (www.pharmacist.com)

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

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

		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	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Names identified in the previous DMEPA review as having some similarity to Vibativ and that have not had changes to their product characteristics

Proprietary Name	Similarity to Vibativ
Vivactil	Look
Vibratabs	Look
Zebeta	Look
Vivotif-Verna	Sound and Look

Appendix C: Proprietary names that lack convincing orthographic and/or phonetic similarities

Proprietary Name	Similarity to Vibativ
Vibion	Look
Vibhitaki	Look
Vigabatrin	Look and Sound

Appendix D: Name that is a trademark for a type of intravenous bag/plastic container that would not be included on a patient order

Proprietary Name	Similarity to Vibativ
Viaflex	Look

Appendix E: Proprietary names in DSS that have been withdrawn by the Commissioner

Proprietary Name	Similarity to Vibativ	Date Withdrawn
Vibelve	Look	July 24, 1970
Vibalt	Look	July 24, 1970

Appendix F: Proprietary names that are internationally registered

Proprietary Name	Similarity to Astepro	Active Ingredient	Country
Vibeden	Look	Hydroxocobalamin (Vit B12)	Denmark
Vibeline	Look	Visnadine	Spain
Vibolex	Look	Vitamin B Substances	Germany
Vibetrat	Look	Vitamin B substances	Brazil
Vibovit	Look and Sound	Multi-vitamin preparation	Poland
Vibovit C	Look and Sound	Vitamin C	Poland
Vibazine	Look	Doxycycline hyclate	India

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

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Vibativ (Telavancin for injection)		**250 mg and 750mg**	**10 mg/kg administered over a 60 minute period by intravenous infusion once every 24 hours for 7 to 14 days**
Reloxin***	Look		
Vitafol Multi-vitamin with minerals	Look	Multivitamin	One caplet by mouth daily

b(4)

Appendix H: Products with potential numerical overlap or similarity in strength and/or dose but multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Vibativ **(Telavancin for injection)**	Look	**250 mg and 750mg**	**10 mg/kg administered over a 60 minute period by intravenous infusion once every 24 hours for 7 to 14 days**	
Zorbtive Somatropin (rhGH) Powder for Injection Short bowel syndrome in patients receiving specialized nutrition support as directed by a health care professional	Look	8.8 mg	0.1 mg/kg subcutaneously once weekly for four weeks	Route of Administration: Intravenous vs. Subcutaneous Dosing Frequency: Once daily vs. once weekly Dose: 10 mg/kg vs. 0.1 mg/kg

b(4)

Appendix I: Products with potential confusion due to overlap in dose and/or strength and/or look-alike or sound-alike concerns

Vibativ (Telavancin for injection)	**Strength 250 mg and 750mg**	**Usual dose: 10 mg/kg administered over a 60 minute period by intravenous infusion once every 24 hours for 7 to 14 days**
Failure Mode:	**Causes (could be multiple)**	**Effects**
Relafen Nabumetone tablets 500 mg and 750 mg 1000 mg orally once or twice daily, an additional 500 mg to 1000 mg may be taken.	Orthographic similarities: Lower case 'r' in Relafen looks similar to the lower case 'v' in Vibativ. Both names are seven letters long with upstrokes in the third and fifth positions. '-fen' of Relafen looks similar to '-tiv' of Vibativ when scripted. Overlapping numeric strengths: 750 mg Overlapping dose: 1000 mg for a 100 kg person vs. 1000 mg	Medication error unlikely due to differing routes of administration and variations in storage conditions, usual dose, route of administration, duration of therapy and rate of administration. *Rationale:* Although doses of 500 mg and 1000 mg could conceivably be achieved with Vibativ. There are differences in their dosage forms (Injection vs. Tablet) and routes of administration (Intravenous vs. Oral).
Rebetol Ribavarin capsules: 200 mg Ribavarin Oral Solution: 40 mg/mL 1000 mg orally broken into two doses daily: Less than or equal to 75 kg: 400 mg in the morning, then 600 mg in the evening Greater than 75 kg: 600 mg in the morning ,then 400 mg in the evening Given in combination with Intron A	Orthographic Similarities: Lower case 'r' in Rebetol looks similar to lower case 'v' in Vibativ. Both names are seven letters long with upstrokes in the third and fifth positions. In addition, the '-to-' of Rebetol can look similar to the '-ti-' of Vibativ when scripted. Overlapping dose: 600 mg for a 60 kg person and 400 mg for a 40 kg person vs. 600 mg and 400 mg	Medication error unlikely due to differing routes of administration and variations in, dosage form, route of administration and dosing frequency. *Rationale:* Although doses of 400 mg and 600 mg could conceivably be achieved with Vibativ. There are differences in their dosage forms (Injection vs. Capsules and Oral Solution).
Librium Chlordiazepoxide Powder for Injection: 100 mg Capsules: 5 mg, 10 mg and 25 mg 50 mg to 100 mg intravenously or intramuscularly; then 25 mg to 50 mg three to four times daily, if necessary 5 mg to 10 mg orally three to four times daily for mild to moderate symptoms 20 mg to 25 mg three to four times daily for severe symptoms	Orthographic similarities: The beginning letters of Vibativ ('Viba-') can look similar to the beginning letters of Librium ('Libr-'). Similar numeric strengths: 250 mg vs. 25 mg 100 mg/kg vs. 10 mg Potential overlap in dose: 1000 mg for a 100 kg persons vs. 10 mg or 100 mg	Medication error unlikely due orthographic differences in the name and differing doses, dosage forms, route of administration and recommended times to administer the dose. *Rationale:* The risk for medication error is minimized by the orthographic differences in the name, Although the names begin with letters that resemble each when written ('Viba-' vs. 'Libr-'), the upstroke of the letter 't' in Vibativ helps to differentiate the two names from each other. While the two products have the same dosage form (injection), route of administration (intravenous) and numeric similarity in strength, The rate of administration (Intravenous infusion over 60 minutes for Vibativ vs. slow intravenous push over 1 minute for Librium), and dosing frequency (Once daily vs. Three to four times daily) of Vibativ and Librium vary significantly.

Relistor Methylnatrexone bromide solution Opiate agonist-induced constipation in patients with advanced illness who are receiving palliative care when response to laxative therapy has been insufficient 0.15 mg/kg to 12 mg subcutaneously every other day	Orthographic similarities:: Lower case 'r' in Relistor looks similar to lower case 'v' in Vibativ.. In addition, the '-listor-' of Relistor can look similar to the 'bativ-' of Vibativ when scripted. Potential overlap in dose: 10 mg for a 1 kg person vs. 10 mg	Medication error unlikely due to differing doses, dosage forms and route of administration. *Rationale:* Even though the doses could overlap at 10 mg, this corresponds to a patient weighing 1 kg and Vibativ is not indicated in neonates. Additionally, the two drugs differ in the routes of administration (Intravenous vs. Subcutaneous) and dosing frequency (once daily vs. every other day).

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/s/

Denise Toyer
11/26/2008 04:17:10 PM
DRUG SAFETY OFFICE REVIEWER

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; White Oak 22; Mail Stop 4447)

DATE RECEIVED: April 26, 2007 **DATE OF DOCUMENT:** April 17, 2007	**DESIRED COMPLETION DATE:** July 31, 2007 **PDUFA DATE:** October 19, 2007	**OSE CONSULT #:** 2007-964

TO: Janice Soreth, MD
Director, Division of Anti-Infective and Ophthalmologic Products

THROUGH: Kristina Arnwine, PharmD., Acting Team Leader
Denise Toyer, PharmD., Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Linda M. Wisniewski, RN, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME: Vibativ (Telavancin for Injection) 250 mg and 750 mg **NDA #:** 22-110	**NDA SPONSOR:** Theravance, Inc.

RECOMMENDATIONS:

1. DMETS does not recommend use of the proprietary name, Vibativ.

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, Vibativ, 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 all correspondence with the sponsor regarding this consult. 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
HFD-420; WO 22; Mail Stop 4447
Center for Drug Evaluation and Research

Proprietary Name Review, Label, and Labeling Review

DATE OF REVIEW: May 14, 2007

NDA #: 22-110

NAME OF DRUG: Vibativ
(Telavancin for Injection)
250 mg and 750 mg

NDA HOLDER: Theravance, Inc.

*****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 Ophthalmologic Products (HFD-520), for assessment of the proprietary name, Vibativ, regarding potential confusion with other proprietary or established drug names. The sponsor initially submitted the proposed name, ( ), for review and comment. However, DDMAC objected to the use of the name ( ) because it 'broadens the indication of the drug product'. The Division concurred with DDMAC's objection. Subsequently, the sponsor submitted the name Vibativ for consideration. Container labels and carton and insert labeling were provided for review and comment. b(4)

PRODUCT INFORMATION

Vibativ is a lipoglycopeptide antibiotic indicated for the treatment of patients with complicated skin and skin structure infections (cSSI) caused by susceptible strains of the following gram-positive microorganisms: *Staphlococcus aureus* (MRSA and MSSA), *Streptococcus pyogenes*, *Streptococcus agalactiae, Streptococcus anginosis* group, and *Enterococcus faecalis*.

The recommended dosing for Vibativ is 10 mg/kg administered over a 60 minute period by intravenous infusion once every 24 hours for 7 to 14 days. Dosage adjustment for patients with moderate or severe renal impairment is as follows: Creatinine clearance of >50 mL/min: 10 mg/kg every 24 hours, 30-50 mL/min: 7.5 mg/kg every 24 hours, and <30 mL/min ( ) 10 mg/kg every 48 hours. b(4)

Vibativ requires reconstitution and further dilution prior to administration. The reconstitution is done with 15 mL of 5% Dextrose Injection, USP; Sterile Water for Injection, USP, or 0.9% Sodium Chloride Injection, USP, to achieve an initial concentration of 15 mg/mL. The reconstituted Vibativ must be further diluted into 100 mL to 250 mL of the appropriate solution to a final dosing concentration of 0.6 mg to 8 mg/mL. Appropriate infusion solutions include: 5% Dextrose Injection, USP; 0.9% Sodium Chloride Injection, USP; or Lactated Ringer's Injection, USP.

The reconstituted medication is stable as long as the total time in the vial plus the time in the intravenous bag does not exceed ( ) hours at room temperature and 72 hours under refrigeration. Other intravenous substances, additives, or other medications should not be added to Vibativ or infused simultaneously through the same intravenous line. If the line is to be used for infusing other medications, the line should be flushed before and after infusion of Vibativ with 5% Dextrose Injection, USP; 0.9% Sodium Chloride Injection, USP; or Lactated Ringer's Injection, USP. b(4)

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 Vibativ 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] 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 (inpatient and outpatient) 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 product 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 Vibativ. 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 did not have concerns with the name Vibativ, in regard to promotional claims.

2. The Expert Panel identified sixteen proprietary names that were thought to have the potential for confusion with Vibativ.

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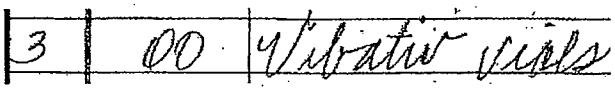
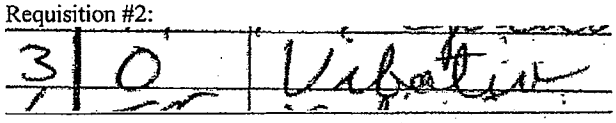
[1] MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, 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

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 Vibativ 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 123 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Two requisitions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Vibativ (see below). These requisitions were optically scanned and one requisition was delivered to a random sample of the participating health professionals via e-mail. In addition, a requisition was recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal requisitions, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN REQUISITION	VERBAL REQUISITION
Requisition #1:  Requisition #2: 	Code 00 Vibativ 3 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 Vibativ, sixteen names were identified as having the potential to sound or look similar to Vibativ. These names include Ribavirin, Revatio, Viactiv, Vivactil, Zebeta, Proactiv, Ultiva, Vibramycin, Vibra-Tabs, Mycobutin, Rifater, Vasotec, Rifadin, Vivotif-Verna, Vibact, and Viviant.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name, Vibativ, could be confused with any of 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.

Upon analysis of the sixteen names, DMETS determined the following fourteen names, Ribavirin, Revatio, Viactiv, Vivactil, Zebeta, Proactiv, Ultiva, Vibramycin, Vibra-Tab, Mycobutin, Vasotec, Vivotif-Verna, Vibact, and Viviant will not be reviewed further for the following reasons:

1. Ribavirin was not considered further because this name pair lacks convincing look-alike properties, as well as having differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 800 mg to 1200 mg), frequency of administration (once daily or once every two days vs. twice daily), route of administration (intravenous vs. oral), and dosage form (injection vs. capsule and tablet).
2. Revatio was not considered further because this name pair lacks convincing look-alike properties, as well as having differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 20 mg), frequency of administration (once daily or once every two days vs. three times a day), dosage form (injection vs. tablet), and route of administration (injection vs. oral).
3. Viactiv was not considered further because this name pair lacks convincing look-alike and sound-alike properties, as well as the fact that Viactiv is a family trade name for a variety of dietary supplements and vitamins (Viactiv Calcium Soft Chews, Viactiv for Teens, Viactiv Calcium Flavor Glides, Viactiv Multivitamin Flavor Glides, and Viactiv Multivitamin Chews). Practitioners must specify which product is to be dispensed.
4. Vivactil was not considered further because this name pair lacks convincing look-alike properties, as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 5 mg/day to 60 mg/day), frequency of administration (once daily or every two days vs. three to four times a day), product strength (250 mg and 750 mg vs. 5 mg and 10 mg), dosage form (injection vs. tablet), and route of administration (intravenous vs. oral).
5. Zebeta was not considered further because this name pair lacks convincing sound-alike properties, as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 2.5 mg to 20 mg), strength (250 mg and 750 mg vs. 1 mg and 10 mg), and route of administration (intravenous vs. oral).
6. Proactiv was not considered further because this name pair lacks convincing sound-alike properties, as well as the fact that Proactiv is a name of an over-the-counter skin care product line consisting of Proactiv Renewing Cleanser, Proactiv Revitalizing Toner, Proactiv Repairing Lotion, Proactiv Oil Free Moisture With SPF 15, and Proactiv Daily Oil Control. Additionally, it is not available in pharmacies, and is usually obtained over the internet or by mail order.
7. Ultiva was not considered further because this name pair lacks convincing look-alike properties as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 0.025 mcg/kg/min to 1 mcg/kg/min), product strength (250 mg and 750 mg vs. 1 mg, 2 mg,a nd 5 mg) and frequency of administration (once daily vs. continuously).
8. Vibramycin was not considered further because this name pair lacks convincing look-alike properties as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 100 mg, 2.2 mg/kg to 4.4 mg/kg), product strength (250 mg and 750 mg vs. 25 mg/5 mL, 50 mg/5 mL, 50 mg, and 100 mg), dosage form (injection vs. oral suspension, capsule, and tablet), and route of administration (intravenous vs. oral). Although it would be possible for the dose to overlap at a dose of 100 mg, the routes of administration (intravenous vs. oral) would help to differentiate these two drugs.
9. Vibra-Tabs was not considered further because this name pair lacks convincing look-alike properties as well as differentiating product characteristics, such as usual dose (7.5 mg/kg

to 10 mg/kg vs. 100 mg), dosage form (injection vs. tablet), product strength (250 mg and 750 mg vs. 100 mg), and route of administration (intravenous vs. oral).

10. Rifabutin was not reviewed further because this name pair lacks convincing look-alike properties as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 300 mg), dosage form (injection vs. capsule), product strength (250 mg and 750 mg vs. 150 mg), and route of administration (intravenous vs. oral).
11. Vasotec was not reviewed further because this name pair lacks convincing look-alike properties as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 10 mg to 40 mg), dosage form (injection vs. tablet and injection), product strength (250 mg, and 750 mg vs. 2.5 mg, 5 mg, 10 mg, and 20 mg), and route of administration (intravenous vs. oral and injection).
12. Vivotif-Verna was not reviewed further because this name pair lacks convincing look-alike and/or sound-alike properties as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. one capsule), frequency of administration (once daily vs. once every other day for four days), and route of administration (intravenous vs. oral).
13. Vibact was not reviewed further because it is a foreign drug in Korea.
14. Viviant[7] was not reviewed further because it lacks convincing look-alike and sound-alike properties as well as differentiating product characteristics, such as usual dose (7.5 mg/kg to 10 mg/kg vs. 20 mg or 40 mg), dosage form (injection vs. tablet), route of administration (intravenous vs. oral), and product strength (250 mg and 750 mg vs. 20 mg or 40 mg).

The remaining two names, Rifadin and Rifater, along with the dosage forms available and usual dosage, are listed in Table 1 (see below).

Table 1: Names Requiring Further Analysis

Product Name	Dosage form (s); Established name	Usual adult dose*	Other**
Vibativ	Telavancin Hydrochloride for Injection 25 mg and 750 mg	Recommended starting dose: 10 mg/kg over 60 minutes by intravenous infusion once every 24 hours for 7-14 days. Creatinine Clearance adjustments: >50 mL/min: 10 mg/kg every 24 hours 30-50 mL/min: 7.5 mg/kg every 24 hours <30 mL/min and hemodialysis: 10 mg/kg every 48 hours	NA
Rifadin	Rifampin Capsules 150 mg and 300 mg Rifampin for Injection 600 mg	Tuberculosis: Adults: 10 mg/kg as a single daily dose, with a maximum 600 mg/day oral or intravenous dose. Pediatrics: 10 mg/kg to 20 mg/kg, not to exceed 600 mg/day. Meningococcal Carriers: Adults 600 mg twice daily for two days. Pediatric doses: >1 month of age: 10 mg/kg q 12 for two days <1 month of age: 5 mg/kg q 12 for two days	LA
Rifater	Rifampin, Isoniazid, and Pyrazinamide Tablets 120 mg/50 mg/300 mg	<44 kg total body weight – 4 tablets 45-54 kg total body weight – 5 tablets >55 kg total body weight – 6 tablets	LA

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

DMETS has the following comments in review of the names Rifadin and Rifater.

1. Rifadin looks similar to Vibativ when written. Rifadin is used to treat tuberculosis and meningococcal carriers.

   The orthographic similiarity stems from the similar looking letters that begin each name, particularly if they are scripted using lower case letters (vib vs. rif and adin vs. ativ). The identical number of letters (7) and similar placement of the upstrokes (third and fifth positions) in each name adds additional orthographic similarity. Although the letter 'f' in Rifadin has an additional downstroke for the below-the-line portion of the letter, it may not be clearly scripted and appear to be the lower loop of the letter 'b' in Vibativ.

   Vibativ and Ridadin share some overlapping product characteristics, such as usual dose (10 mg/kg), frequency of administration (once daily), route of administration (intravenous), dosage form (injection), and pharmacological classification (antibiotic). The orthographic similarities and overlapping product characteristics provide increased opportunity for error involving these two products. Therefore, DMETS does not recommend use of the name Vibativ.

   rifadin 600 mg IV QD
   ribativ 600 mg IV QD

2. Rifater was identified as a name that may look similar to Vibativ when written. Rifater is used to treat pulmonary tuberculosis.

   Both Rifadin and Vibativ contain letters that may look similar when scripted, particularly if they are scripted using lower case letters (vib vs. rif and ater vs. ativ). The identical number of letters (7) and similar placement of the upstrokes (third and fifth positions) in each name adds additional orthographic similarity. Although the 'f' of Rifater has an additional downstroke for the below-the-line portion of the letter, it may not be clearly scripted and appear to be the lower loop of the letter 'b' in Vibativ.

   Although both products are administered once daily, there are product characteristics that will help to differentiate these two names. These include dose (7.5 mg/kg to 10 mg/kg vs. 4 tablets, 5 tablets, and 6 tablets), route of administration (intravenous vs. oral), dosage form (injection vs. tablet), and strength (250 mg and 750 mg vs. 50 mg/300 mg/120mg). Thus, the dose, route of administration, dosage form, and context of use (weight-based dosing vs. standard dosing) will help to differentiate these two products when ordered.

   rifater
   vibater

III. COMMENTS TO THE SPONSOR:

DMETS does not recommend the use of the proprietary name, Vibativ because of its orthographic similarity to Rifadin.

Rifadin looks similar to Vibativ when written. Rifadin is used to treat tuberculosis and meningococcal carriers.

The orthographic similiarity stems from the similar looking letters that begin each name, particularly if they are scripted using lower case letters (vib vs. rif and adin vs. ativ). The identical number of letters (7) and similar placement of the upstrokes (third and fifth positions) in each name adds additional orthographic similarity. Although the letter 'f' in Rifadin has an additional downstroke for the below-the-line portion of the letter, it may not be clearly scripted and appear to be the lower loop of the letter 'b' in Vibativ.

Vibativ and Ridadin share some overlapping product characteristics, such as usual dose (10 mg/kg), frequency of administration (once daily), route of administration (intravenous), dosage form (injection), and pharmacological classification (antibiotic). The orthographic similarities and overlapping product characteristics provide increased opportunity for error involving these two products. Therefore, DMETS does not recommend use of the name Vibativ.

rifadin 600 mg IV QD
vibativ 600 mg IV QD

Additionally, DMETS reviewed the labels and labeling form a safety perspective. DMETS has identified the following areas of possible improvement, which may minimize potential user error.

A. GENERAL COMMENT

1. Replace the abbreviation "I.V." with intravenous. The FDA in conjunction with the ISMP launched a campaign on June 14, 2006 to reduce medication errors and/or confusion caused by unclear medical abbreviations. Furthermore, the July 20, 2006 IOM Report titled "Preventing Medication Errors" recommends and urges FDA to standardize abbreviations, acronyms, and terms to the extent possible (i.e., recommendation #4 in the IOM report). Additionally, JCAHO discourages the use of dangerous abbreviations, acronyms, and symbols in their 2006 National Patient Safety Goals of The Joint Commission for Accreditation of Hospitals.

2. Increase the font size of the established name so that it is at least ½ the size of the font of the proprietary name.

3. We note the strength is based on the active moiety, Telavancin, and not the hydrochloride salt. [redacted] For further guidance, DMETS recommends that the Division consult Richard Lostritto, Chair of the CDER Labeling and Nomenclature Committee (LNC), Karl Stiller (the Project Manager assigned to the LNC), and the assigned ONDQA chemist regarding the presentation of the established name for this product. b(4)

4. The DOSAGE AND ADMINISTRATION SECTION, 2.3 Instructions for Intravenous Administration subsection, refers to the resulting concentration after reconstitution as 15 mg/mL. The vials that contain 250 mg and 750 mg are reconstituted with 15 mL and 45 mL of 0.9% Sodium Chloride, respectively. When reconstituted with the identified amount, the calculation results in a ( ) mg/mL concentration. DMETS assumes this difference is due to the chemical properties of the drug. However, this difference in the calculated amounts and the actual amount could result in dosing errors. Since dosing and administration of this product is based on the 15 mg/mL concentration, please include reconstitution instructions on the container and carton labeling. For example: 'Reconstitute with xx mL of xxx solution to result in 15 mg/mL. This needs further dilution in xx ...before administration'. This will help prevent dosing errors based on manual calculations. b(4)

B. CONTAINER LABEL (250 mg and 750 mg)

1. See GENERAL COMMENTS A1 through A4.

2. Include the statement 'Discard Unused portion'.

3. The presentation of the name in all capital letters makes the name difficult to read. DMETS suggests the use of title case letters.

C. CARTON LABELING

See GENERAL COMMENTS A1 through A4 and comments B3 and B4.

D. INSERT LABELING

1. See GENERAL COMMENTS A1, A3, and A4.

2. The information regarding the dilution appears only under the dilution instructions for the 750 mg vial. This gives the appearance that only the 750 mg vial needs a dilution. Revise this section to clearly indicate that both the 250 mg and 750 mg vials require dilution prior to administration.

Appendix A:

Outpatient Written	Verbal	Inpatient Written
Vibatin	Bibactiv	VIBATIN
Vibatin	Vibactive	vibativ
Vibatin	Vivactiv	Vibativ
Vibatin	Vivactiv	Vibativ
Vibatio	Vivactiv	Vibativ
Vibativ	Vivactiv	Vibativ
Vibativ	Vivactiv	Vibativ
Vibativ	Vivactive	Vibativ
Vibativ	Vivactive	Vibativ
Vibativ	Vivactive	Vibativ
Vibativ	Vivactive	Vibativ
Vibotiv	Vivactive	Vibativ
	Vivatif	Vibatrin

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Linda Wisniewski
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DRUG SAFETY OFFICE REVIEWER

Denise Toyer
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