CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125277

PROPRIETARY NAME REVIEW(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

SEP 04 2009

BLA 125277

PROPRIETARY NAME REQUEST CONDITIONALLY ACCEPTABLE

Dyax Corp
300 Technology Square
Cambridge, MA 02139

Attention: Aurelie Grienenberger, PhD
Director of Regulatory Affairs

Dear Dr. Grienenberger:

Please refer to your Biologics License Application (BLA), submitted under section 351 of the Public Health Service Act for Ecallantide Injection, 10 mg/mL.

We also refer to your June 10, 2009, correspondence, received June 10, 2009, requesting review of your proposed proprietary name, Kalbitor. We have completed our review of the proposed proprietary name, Kalbitor, and have concluded that it is acceptable.

The proposed proprietary name, Kalbitor, will be re-reviewed 90 days prior to the approval of the BLA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your June 10, 2009, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Sean Bradley, R.Ph., Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-1332. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

Carol Holquist

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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:	September 4, 2009
To:	Badrul Chowdhury, M.D., Ph.D., Director Division of Pulmonary and Allergy Products
Through:	Kellie Taylor, Pharm.D., M.P.H., Team Leader C Holquist for 9-4-09 Denise Toyer, Pharm.D., Deputy Director C Holquist for 9-4-09 Carol Holquist, R.Ph., Director Carol Holquist 9-4-09 Division of Medication Error Prevention and Analysis
From:	Tara Turner, Pharm.D., Safety Evaluator C Holquist for 9-4-09 Division of Medication Error Prevention and Analysis
Subject:	Final Proprietary Name Review
Drug Name(s):	Kalbitor (Ecallantide) Injection 10 mg/mL
Application Type/Number:	BLA 125277
Applicant:	Dyax Corporation
OSE RCM #:	2009-1220

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1 INTRODUCTION

This review is written in response to the anticipated approval of BLA# 125277 within 90 days from the date of this review.

DMEPA found the proposed name, Kalbitor, acceptable in OSE Review #2008-1684, dated March 11, 2009. Further, the Review Division did not have any concerns with the proposed name during our initial review. Since that review, a Risk Evaluation and Mitigation Strategy (REMS) has been submitted. As part of the proposed REMS, administration of this product will be restricted to healthcare settings that can manage anaphylaxis (e.g. physician office, emergency department). This change in product distribution was considered in the overall assessment of the name.

2 METHODS

2.1 DATABASE AND INFORMATION SOURCES

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see Section 6) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review of Kalbitor. We used the same search criteria outlined in OSE Review #2008-1684. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. Additionally, DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

2.2 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Licensee submitted an external evaluation of the proposed proprietary name. The June 10, 2009 request for proprietary name review includes a summary of an additional analysis performed in 2008 by Addison Whitney to update their initial research. This information was not provided to DMEPA during the first review cycle. However, an evaluation was conducted by Addison Whitney in 2004 and was analyzed as part of DMEPA's original review of the proposed name, Kalbitor (OSE review # 2008-1684).

2.3 COMMENTS FROM DDMAC

DMEPA requests the Division of Drug Marketing, Advertising, and Communications (DDMAC) for their comments or concerns with the proposed proprietary name from the perspective of drug marketing and promotion.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches of the databases yielded two new names thought to look similar to Kalbitor and represent a potential source of drug name confusion. These names are: Kalexate and Raniclor.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of August 25, 2009.

3.2 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

In the 2008 update, Addison Whitney identified and evaluated a total of four drug names thought to have some potential for confusion with the name Kalbitor. One name (Kaletra) was thought to look similar to Kalbitor. One name (Crestor) was thought to sound similar to Kalbitor. The remaining two names (Lipitor and Zaditor) were thought to look and sound similar to Kalbitor. Of the four names, only one (Crestor) was not previously evaluated in our original review of the proposed name.

3.3 COMMENTS FROM DDMAC

On August 18, 2009, DDMAC reviewed the proposed proprietary name and had no concerns from a promotional perspective.

4 DISCUSSION

The revisions in product distribution did not pose any anticipated failure modes. The external study submitted by the Licensee concluded that the proposed name, Kalbitor, has a very low probability of confusion.

In this evaluation, a total of three names were analyzed to determine if the drug names could be confused with Kalbitor and if the drug name confusion would likely result in a medication error.

One name lacked orthographic and/or phonetic similarity and was not evaluated further (see Appendix A). The remaining two names were evaluated using Failure Mode and Effects Analysis (FMEA). The findings of the FMEA indicate that the proposed name, Kalbitor, is not likely to result in name confusion with either of the names for the reasons presented in Appendices B and C.

5 CONCLUSIONS AND RECOMMENDATIONS

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

DMEPA considers this a final review; however, if approval of the BLA is delayed beyond 90 days from the date of this review, the Division of Pulmonary and Allergy 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 Sean Bradley, OSE project manager, at 301-796-1332.

5.1 COMMENTS TO THE LICENSEE

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

6 REFERENCES

1. Turner, Tara. OSE Review #2008-1684: Proprietary Name Review for Kalbitor. 11 March 2009.

2. ***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.

3. ***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.

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

USAN Stems List contains all the recognized USAN stems.

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

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

APPENDICES

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Appendix A: Name lacking convincing look-alike or sound-alike similarities with Kalbitor

Proprietary Name	Similarity to Kalbitor	Source
Crestor	Sound	Addison Whitney (2008 update)

Appendix B: Single Strength Product with Differentiating Product Characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Kalbitor (ecallantide)		Injection 10 mg/mL	30 mg injected subcutaneously (3 injections of 10 mg each) may be repeated once for a total of 60 mg per attack	
Kalexate (sodium polystyrene sulfonate, USP)	Look	Powder : Jars containing 1 lb (454 grams)	Oral: 15 grams one to four times daily, given in a small quantity of water, usually between 20 to 100 mL Rectal: 30 to 50 grams in 100 mL of an aqueous vehicle, such as sorbitol, rectally every six hours	**Dosage form:** Powder vs. solution for injection **Route of administration:** Oral or rectal vs. subcutaneous **Frequency of administration:** 1 to 4 times daily vs. during acute attack, may repeat once

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Appendix C: Product with no overlap in strength or dose

Kalbitor (ecallantide)		Injections: 10 mg/mL	30 mg injected subcutaneously (3 injections of 10 mg each); may be repeated once for a total of 60 mg per attack
Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Raniclor (cefaclor)	Look	Chewable tablets : 125 mg, 187 mg, 250 mg, 375 mg	Adults: 250 mg to 500 mg orally every 8 hours; maximum dose is 2 grams per day Children: 20 mg/kg/day to 40 mg/kg/day in divided doses every 8 hours; maximum dose is 1 gram per day

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:	March 11, 2009
To:	Badrul Chowdhury, M.D., Ph.D., Director Division of Pulmonary and Allergy Products (DPAP)
Through:	Kellie Taylor, Pharm.D., M.P.H., Team Leader 3/11/09 Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director 3/11/09 Division of Medication Error Prevention and Analysis (DMEPA)
From:	Tara Turner, Pharm.D., Safety Evaluator 3/11/09 Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Kalbitor (Ecallantide) Solution for Injection 10 mg/mL
Application Type/Number:	BLA# 125277
Applicant:	Dyax Corporation
OSE RCM #:	2008-1684; 2007-2191

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

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EXECUTIVE SUMMARY

This evaluation raised concerns with the proposed product's established name, Ecallantide, regarding the potential for name confusion with Exenatide (established name for Byetta). This is due to the combination of orthographic similarity and overlapping product characteristics. The Applicant should be made aware of this potentially confusing name pair. We recommend the Applicant discuss this issue with USAN/INN (International Nonproprietary Name) and petition for a new established name. Additionally, we have contacted the FDA USAN representative, David Lewis, on this issue.

With respect to the proposed proprietary name, Kalbitor, we find this to not be vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Kalbitor, for this product.

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 name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change.

In addition, the proposed name must be reevaluated 90 days before approval of the BLA, even if the proposed product characteristics as stated in this review are not altered.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Pulmonary and Allergy Products (DPAP) for an assessment of the proposed proprietary name, Kalbitor, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, the Applicant submitted an independent name analysis prepared by Addison Whitney for review and comment. Container labels, carton and insert labeling were submitted and will be reviewed under separate cover in OSE RCM # 2009-87.

1.2 PRODUCT INFORMATION

Kalbitor (ecallantide) is a product that is being developed for the treatment of acute attacks of hereditary angioedema (HAE). For this indication it is designated as an orphan drug. Kalbitor is intended to be administered by a clinician as a 30 mg subcutaneous dose via injections to the thigh, abdomen, or upper arm to HAE patients. If the patient experiences HAE related swelling in one or more of these injection sites, then the clinician will move the injection(s) to another location. Patients who fail to improve or have an incomplete response or a relapse of symptoms may receive a second dose of 30 mg for a total of 60 mg per attack. The drug product is a sterile, preservative-free solution for subcutaneous injection, formulated at 10 mg/mL with each vial containing 1.15 mL. The product is stored under refrigeration. It will be shipped at refrigerated temperatures in a package containing three vials.

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment (See 2.1 Proprietary Name Risk Assessment). The primary objective for the assessment is to identify and remedy potential sources of medication error prior to drug approval. DMEPA defines a medication error as any preventable event

that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

2.1 PROPRIETARY NAME RISK ASSESSMENT

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.

For the proposed proprietary name, DMEPA staff searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (See 2.1.1 for details) and held a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (See 2.1.1.2). DMEPA staff also conducts internal CDER prescription analysis studies. When provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

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 2.1.2 for details). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] FMEA is used to analyze whether the drug names identified with 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]

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

2.1.1 Search Criteria

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

For this review, particular consideration was given to drug names beginning with the letter 'K' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[4,5]

To identify drug names that may look similar to Kalbitor, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), upstrokes (four, capital letter 'K' and lower case 'l', 'b', and 't'), downstrokes (none), cross-strokes (one, lower case 't') and dotted letters (one, lower case 'i'). Additionally, several letters in Kalbitor may be vulnerable to ambiguity when scripted, including the capital letter 'K' may appear as capital 'R'; lower case 'k' may look like lower case 'h' or 'x'; lower case 'a' may look like lower case 'c'; lower case 'l' may look like lower case 'b', 'e', or 't'; lower case 'b' may look like lower case 'l', 'li', 'h', or 'v'; lower case 'i' may look like lower case 'e'; lower case 't' may look like lower case 'r'; lower case 'o' may look like lower case 'e','a', or 'u'; and lower case 'r' may appear as lower case 'n'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Kalbitor.

When searching to identify potential names that may sound similar to Kalbitor, the DMEPA staff searches for names with similar number of syllables (3), stresses (KAL-bi-tor or kal-BI-tor or kal-bi-TOR), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as the letter 'k' may sound like 'c' or 'q'; the letter 'a' may sound like 'o', the letter 'i' may sound like 'a'; and the letter 't' may sound like 'd'. The Applicant's intended pronunciation of the proprietary name was not provided with the proposed name submission and, therefore, could not be taken into consideration. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

The DMEPA staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names because the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the following information was provided about the proposed product to the medication error staff: proposed proprietary name (Kalbitor), proposed established name (ecallantide), proposed indication of use (treatment of acute attacks of hereditary angioedema), strength (10 mg/mL), dose (30 mg), frequency of administration (maximum of two doses per attack), route (subcutaneous), and dosage form (solution for injection). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

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, these broader safety implications of the name are considered and evaluated throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

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

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

2.1.1.1 Database and Information Sources

The proposed proprietary name was provided to the DMEPA staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 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 used a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff reviewed the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators were then pooled and presented to the CDER Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

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

The pooled results of the DMEPA staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.2 FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ a total of 123 (one hundred twenty-three) healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

Figure 1. Kalbitor Study (conducted on November 30, 2007)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Outpatient Prescription: Kalbitor 30mg #1 Return to clinic for a SQ inj per attack may repeat x1 Dr. [illegible]	"Kalbitor 30 mg #1 Return to clinic for a SQ injection per attack; May repeat x1"
Inpatient Medication Order: Kalbitor 30mg #1 Return to clinic for a SQ injection per attack may repeat PX 1 (one)	

2.1.3 External Proprietary Name Risk Assessment

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

2.1.4 Comments from the Division of Pulmonary and Allergy Products

DMEPA requests the regulatory division in the Office of New Drugs responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. Any comments or concerns are addressed in the safety evaluator's assessment.

The regulatory division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The regulatory division is requested to concur /not concur with DMEPA's final decision.

2.1.5 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies his/her individual expertise gained from evaluating medication errors reported to FDA to conduct 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.[6] 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 as a result of the 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 Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking:

> ***"Is the name Kalbitor 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 Kalbitor 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 possess similarity that would cause confusion at any point in the medication use system, then 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 not ultimately 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; for example, product reformulation to avoid an overlap in strength

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

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 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 proprietary 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 (United States Adopted Names) stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. 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.

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 use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these criteria are met, then DMEPA will not object to the use of the proprietary name. If any of these criteria are met, then DMEPA will object to the use of the proposed proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission (JC), and the Institute for Safe Medication Practices (ISMP), 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 and other post-approval efforts are low-leverage strategies that have proven to have limited effectiveness at alleviating medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for 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).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. 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.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The searches yielded a total of forty-two names as having some similarity to the name Kalbitor.

Twenty-six of the names were thought to look like Kalbitor. These include Habitrol, Kaletra, Zaditor, Limbitrol, Gabitril, (b) (4)***, Felbatol, Kalbron, Kalcidon, Haldol, Halcion, Naldecon, Kalbeten, Kelacal, Albuterol, Relistor, Rifater, Ketalar, Xalatan, Kolester, Kalticol, (b) (4)***, Rebetol, Rebetron, Kalferon, and Kalidren. Seven of the names were thought to sound like Kalbitor. These include Caldecort, Carbachol, Advicor, Altocor, Avicor, Calbital, and Calderol. The remaining nine names were thought to look and sound similar to Kalbitor. These include Carnitor, Kelnor 1/35, Carbatrol, (b) (4)***, (b) (4)***, Lipitor, Zalditor, Kalicor, and Kolestor.

Our searches also revealed that the proposed name, Kalbitor, is trademarked in many foreign countries. All of these trademarks, with the exception of Japan, are registered to Dyax Corporation.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of January 23, 2009.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1.1 above) and identified one additional name, Exenatide, as having look-alike similarity with Ecallantide (the established name for Kalbitor).

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

3.1.3 FDA Prescription Analysis Studies

A total of 34 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Approximately 85% of the participants (n=29) interpreted the name correctly as "Kalbitor", with the correct interpretation occurring more frequently in the inpatient written study. The remainder of participants misinterpreted the drug name. The most common misinterpretations involved the misinterpretation of the letter 'K' as 'C' alone (Calbitor) or in combination with the misinterpretation of the letter 'i' as 'a' (Calbator). See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 External Proprietary Name Risk Assessment

In the proposed name risk assessment submitted by the Applicant, Addison Whitney identified and evaluated a total of five drug names thought to have some potential for confusion with the name Kalbitor. Two of the names (Kabitrol and Kaletra) were thought to look similar to Kalbitor. Two of the names (Carnitor and Zocor were thought to sound similar to Kalbitor. The remaining name, Lipitor, was thought to look and sound similar to Kalbitor. Two of the five names (Zocor and Kabitrol) were not previously identified in our Staff searches or the Expert Panel Discussion.

Addison Whitney found the name, Kalbitor, acceptable.

3.1.5 Comments from the Division of Pulmonary and Allergy Products (DPAP)

DMEPA notified DPAP via e-mail that we had no objections to the proposed proprietary name, Kalbitor, on February 26, 2009. Per e-mail correspondence from DPAP on February 26, 2009, they indicated they concur with our assessment of the proposed proprietary name, Kalbitor.

3.1.6 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator resulted in 5 additional names which were thought to look or sound similar to Kalbitor and represent a potential source of drug name confusion. The names identified to have look-alike similarities are: Thalitone, Halotex, Kaloba, and Halitol. The remaining name, (b) (4)***, was identified to have sound-alike similarities.

Additionally, we note that attempts to identify the drug names, Zalditor and Kabitrol, were unsuccessful. We assume that these names were misspelled during the search process (i.e. Zalditor for Zaditor and Kabitrol for (b) (4) Thus, we evaluated Zaditor and (b) (4) (already identified in section 3.1.1 above).

Forty-seven names were analyzed to determine if the drug names could be confused with Kalbitor and if the drug name confusion would likely result in a medication error.

Thirteen names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix C).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with any of the remaining thirty-four names and lead to medication errors. This analysis determined that the name similarity between Kalbitor and the identified names was unlikely to result in medication errors with any of the thirty-four products identified for the reasons presented in Appendices D through J.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

Forty-seven names were evaluated for their potential similarity to the proposed name, Kalbitor. The FMEA indicates that the proposed name is not likely to result in name confusion that could lead to medication errors. This finding is consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

We also noted that the established names Ecallantide and Exenatide have orthographic similarities. This is due to the fact that the names begin with the letter 'E' and they have similar endings ('antide' vs. 'atide'). Additionally, Ecallantide and Exenatide share several overlapping product characteristics: dose (3 injections of 10 mg each vs. 5 or 10 micrograms); route of administration (subcutaneous injection to the thigh, abdomen, or upper arm); dosage form (solution for subcutaneous injection); and storage

conditions (refrigerate and protect from light). Given these considerations, there is increased risk of confusion between this pair of established names.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Kalbitor, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Kalbitor, for this product at this time. Additionally, DDMAC does not object to the proposed name, Kalbitor, from a promotional perspective.

However, we have concerns with the proposed product's established name, Ecallantide, regarding the potential for name confusion with Exenatide (established name for Byetta). This is due to the combination of orthographic similarity and overlapping product characteristics. The Applicant should be made aware of this potentially confusing name pair. We recommend the Applicant discuss this issue with USAN/INN (International Nonproprietary Name) and petition for a new established name. Additionally, we have contacted the FDA USAN representative, David Lewis, on this issue.

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 name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

5.1 COMMENTS TO THE DIVISION

The established name is set by the United States Adopted Names (USAN) Council. The FDA USAN representative and the Applicant should be made aware of this potentially confusing name pair.

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

5.2 COMMENTS TO THE APPLICANT

5.2.1 Proprietary Name

We have completed our review of the proposed proprietary name, Kalbitor, and have concluded that it is acceptable. Kalbitor will be re-reviewed 90 days prior to the approval of the BLA. If we find the name unacceptable following re-review, we will notify you.

Additionally, we note that your proposed established name is orthographically similar to the established name Exenatide. The orthographic similarity has the potential to contribute to error due to the fact that the names begin with the letter 'E' and they have similar endings ('antide' vs. 'atide'). Additionally, Ecallantide and Exenatide share several overlapping product characteristics: dose (3 injections of 10 mg each vs. 5 or 10 micrograms); route of administration (subcutaneous injection to the thigh, abdomen, or upper arm); dosage form (solution for subcutaneous injection); and storage conditions (refrigerate and protect from light). Given these considerations, there is increased risk of confusion between this pair of established names. We recommend you discuss this issue with USAN/INN (International Nonproprietary Name) and petition for a new established name.

6 REFERENCES

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

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

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

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

3. *Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)*

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

4. *AMF Decision Support System [DSS]*

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

The medication error staff 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 names 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 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 medication error 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), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (See Table 1 below for details). In addition, the medication error 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.

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-strokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

		Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B:

Kalbitor Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Medication Order
Kalbitan	calbator	kalbitor
Kalbitor	Calbator	Kalbitor
Kalbitor	Calbitor	Kalbitor
Kalbitor	Calbitor	Kalbitor
Kalbitor		Kalbitor
Kalbitor		Kalbitor
Kalbitor		Kalbitor
Kalbitor		KALBITOR
Kalbitor		Kalbitor
Kalbitor		Kalbitor
Kalbitor		Kalbitor
Kalbitor		Kalbitor
Kalbitor		
Kalbitor		
Kalbitor		
Kalbitor		
Kalbitor		
Kalbitor		

Appendix C: Names lacking convincing look-alike or sound-alike similarities with Kalbitor

Proprietary Name	Similarity to Kalbitor
Limbitrol	Look
Gabitril	Look
(b) (4)***	Look
Naldecon	Look
Lipitor	Look and Sound
Zocor	Sound
(b) (4)***	Look
Albuterol	Look
Carbachol	Sound
Advicor	Sound
(b) (4)***	Sound
(b) (4)***	Sound
Calderol	Sound

Appendix D: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Kalbitor	Countries	Description
Kalbron	Look	Indonesia	Theophylline capsules and syrup
Kalcidon	Look	Sweden; Finland	Calcium carbonate
Kalbeten	Look	Israel	Bismuth subsalicylate tablets and suspension
Kalticol	Look	Indonesia	Thiamphenicol
Kalferon	Look	Indonesia	Interferon alfa-2b
Kalidren	Look	Turkey	Diclofenac

Kalicor	Look and Sound	Czech Republic	Piracetam
Kolestor	Look and Sound	Turkey	Atorvastatin
Kaloba	Look	Brazil; Venezuela; Netherlands; United Kingdom	Pelargonium sidoides (Geranium oil)

Appendix E: Proposed proprietary names that have never been marketed in the U.S.

Proprietary Name	Similarity to Kalbitor	Description	Status
			(b) (4)

Appendix F: Products that are not currently marketed in the U.S.

Proprietary Name	Similarity to Kalbitor	Description	Status
Halotex	Look	Haloprogin cream 1% and Topical solution 1%	Discontinued (no generics available)
Calbital Tab	Sound	No information	Withdrawn by Commissioner (as of July 24, 1970)
Halitol Mouthwash	Look	No information	Withdrawn by Commissioner (as of July 24, 1970)

Appendix G: Natural medicine product

Proprietary Name	Similarity to Kalbitor	Description
Kolester	Look	Okra/ Male Fern/ Beth root/ Rhubarb root/ Calamus root

Appendix H: Products with no overlap in strength or dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Kalbitor **(ecallantide)** **solution for injection**		**10 mg/mL**	**30 mg injected subcutaneously (3 injections of 10 mg each); may be repeated once for a total of 60 mg per attack**
Zaditor (ketotifen)	Look	Ophthalmic solution: 0.025%	Instill one drop into the affected eye(s) every 8 to 12 hours, no more than twice per day.
Felbatol (felbamate)	Look	Tablet: 400 mg, 600 mg Oral Solution: 600 mg/5 mL	1200 mg per day in 3 to 4 divided doses orally; increase the dosage in 600 mg increments every 2 weeks to 2400 mg per day based on clinical response and thereafter to 3600 mg per day if clinically indicated.
Halcion (triazolam)	Look	Tablet: 0.125 mg; 0.25 mg	0.25 mg before retiring
Caldecort (hydrocortisone acetate) cream	Sound	Cream: 1%	Apply no more than 3 to 4 times daily.
Kelnor 1/35 (ethinyl estradiol/ethynodiol acetate)	Look and Sound	21 active tablets (ethinyl estradiol 0.035 mg/ ethynodiol diacetate 1 mg) 7 inert tablets	One tablet orally once daily.
Relistor (methylnaltrexone)	Look	Injection: 12 mg/0.6 mL	The usual schedule is one dose every other day, as needed, but no more frequently than one dose in a 24 hour period. The recommended dose is 8 mg for patients weighing 38 to less than 62 kg or 12 mg for patients weighing 62 to 114 kg. Patients whose weights fall outside of these ranges should be dosed at 0.15 mg/kg.
Rifater (rifampin/isoniazid/pyrazinamide)	Look	Tablet: rifampin 120 mg/ isoniazid 50 mg/	Patients should be given the following single daily dose either 1 hour before or 2 hours after a meal with a full glass

		pyrazinamide 300 mg	of water: Patients weighing ≤ 44 kg: 4 tablets Patients weighing between 45 and 54 kg: 5 tablets Patients weighing ≥ 55 kg: 6 tablets
Xalatan (latanoprost)	Look	Ophthalmic solution: 0.005%	One drop in the affected eye(s) once daily in the evening.
Rebetol (ribavirin)	Look	Capsule: 200 mg Oral Solution: 40 mg/mL	In combination with Intron A: For patients weighing ≤ 75 kg: 400 mg AM and 600 mg PM orally daily For patients weighing >75 kg: 600 mg AM and 600 mg PM orally daily In combination with PegIntron: 400 mg AM orally with food and 400 mg PM orally with food daily.
Rebetron	Look	Rebetol (ribavirin) Capsules: 200 mg and Intron A (interferon alfa-2b recombinant) Injection:	*Intron® A:* Subcutaneous: 3 million international units 3 times/week **and** *Rebetol® capsule:* Oral: ≤75 kg (165 pounds): 1000 mg/day (two 200 mg capsules in the morning and three 200 mg capsules in the evening) >75 kg: 1200 mg/day (three 200 mg capsules in the morning and three 200 mg capsules in the evening)
Carnitor (levocarnitine)	Look and Sound	Tablets: 330 mg Oral Solution: 1 gram per 10 mL Sugar Free Oral Solution: 1 gram per 10 mL Injection: 1 gram per 5 mL vial or ampule	Tablets: 990 mg orally two or three times a day Oral Solution: 1 to 3 grams orally per day, which is equivalent to 10 to 30 mL per day Injection: 50 mg/kg given as a slow 2 to 3 minute bolus injection or by intravenous infusion. Often a loading dose is given in patients with severe metabolic crisis followed by an equivalent dose over the following 24 hours. It should be administered every 3 hours or every 4 hours, and never less than every 6 hours, either by infusion or by IV injection. All subsequent daily doses are recommended to be in the range of 50 mg/kg or as therapy may require. The highest dose administered has been 300 mg/kg.
Carbatrol	Look and Sound	Extended release capsules:	Initial dose is 200 mg orally twice daily; may adjust dosage to minimum

(carbamazepine)		100 mg, 200 mg, 300 mg	effective level, usually 800 mg to 1200 mg daily.
Thalitone (chlorthalidone)	Look	Tablets: 15 mg (25 mg discontinued – not interchangeable with other chlorthalidone products)	Hypertension: Initiate at 15 mg orally once daily; increase if needed to 30 mg orally once daily, then to 45 to 50 mg once daily Peripheral Edema: Initiate at 30 mg to 60 mg orally daily or 60 mg orally on alternate days

Appendix I: Products with overlap in strength or dose.

Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**
Kalbitor (ecallantide) solution for injection	**10 mg/mL**	**30 mg injected subcutaneously (3 injections of 10 mg each); may repeat once for a total of 60 mg per attack**
Haldol (haloperidol) tablets: 0.5mg, 1 mg, 2 mg, 5 mg, 10 mg, 20 mg - brand name products discontinued; generics available (haloperidol lactate) oral concentrate: 2 mg/mL- brand name product discontinued; generics available (haloperidol lactate) injection: 5 mg/mL (haloperidol decanoate) injection: 50 mg/mL, 100 mg/mL	Orthographic similarity Numerically similar strengths (10 mg/mL vs. 100 mg/mL)	Although the names begin with letters that may look similar when scripted ('Kal' vs. 'Hal'), the remaining letters do not look alike which helps to differentiate the names. Additionally, Kalbitor contains 8 letters and appears longer when scripted compared to Haldol which contains 6 letters. Haldol is available in both oral and parenteral dosage forms. The oral dose ranges from 0.5 to 2 mg two to three times per day for moderate symptoms or 3 mg to 5 mg two to three times per day for severe symptoms. Daily dosages up to 100 mg may be necessary. The immediate acting parenteral dose ranges from 2 to 10 mg administered intramuscularly and may be repeated at 1 hour intervals. The intramuscular depot formulation dose is based on the patient's oral dose and is administered once per month. In contrast, Kalbitor is available as a solution for subcutaneous injection in a single concentration, 10 mg/mL. The recommended dose is 3 injections of 10 mg each administered subcutaneously, for a total of 30 mg, in an acute attack.
Ketalar (ketamine) Injection 10 mg/mL; 50 mg/mL; 100 mg/mL	Orthographic similarity Overlapping strength (10 mg/mL)	Although the names both begin with the letter 'K' and have similar endings ('lar' vs. 'tor'), the middle letters help to differentiate them. The 'alb' in Kalbitor makes that name look longer than Ketalar when scripted.

		Ketalar is administered intravenously for the induction and maintenance of anesthesia. The dose is individualized based on the patient's weight and anesthetic needs. By contrast, Kalbitor has a fixed dose of 30 mg and is administered as 3 subcutaneous injections of 10 mg each for acute attacks of hereditary angioedema.

(b) (4)

Appendix J: Strong orthographic similarity but no overlap in strength or dose.

Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**
Kalbitor (ecallantide) solution for injection	**10 mg/mL**	**30 mg injected subcutaneously; may receive a total of 60 mg per attack**
(b) (4)	Orthographic similarity (b) (4)	Medication errors are unlikely in the usual practice setting. (b) (4) In contrast, Kalbitor is available as a solution for subcutaneous injection. The 30 mg dose must be administered by a healthcare provider in the clinic or hospital setting for acute attacks of hereditary angioedema.
Kaletra (lopinavir/ritonavir) Film-coated tablets: 200 mg/50 mg, 100 mg/25 mg Oral solution: 80 mg/20 mg per mL Capsules: 133.3mg/33.3 mg	Orthographic similarity Kaletra Kalbitor	Medication errors are unlikely in the usual practice setting. Kaletra is a drug product used for the treatment of HIV infection. It is an oral product which is administered once or twice daily. In contrast, Kalbitor is available as a solution for subcutaneous injection. The 30 mg dose must be administered by a healthcare provider in the clinic or hospital setting for acute attacks of hereditary angioedema.