CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-465

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:	September 24, 2009
To:	Robert Justice, MD, Director Division of Drug Oncology Products
Through:	Kristina Arnwine, Pharm.D., Team Leader Denise Toyer, Pharm.D., Deputy Director Division of Medication Error Prevention and Analysis
From:	Lori Cantin, RPh, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Votrient (Pazopanib)
Application Type/Number:	NDA 22465
Applicant:	GlaxoSmithKline
OSE RCM #:	2009-908

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

1 INTRODUCTION

This re-assessment of the proprietary name is written in response to notification that NDA 22465 may be approved within 90 days. DMEPA found the proposed proprietary name, Votrient, acceptable in OSE Review #2009-177, dated May 6, 2009. The Division of Drug Oncology Products did not have any concerns with the proposed name, Votrient, and the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective in the May 6, 2009, review.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. We use the same search criteria that were used in OSE Review# 2009-177 for the proposed proprietary name, Votrient. 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.

The searches of the databases yielded three new names, (b) (4) thought to look similar to Votrient and represent a potential source of drug name confusion. These names were evaluated using FMEA. The findings of the FMEA indicate that the proposed name, Votrient, is not likely to result in name confusion with (b) (4) for the reasons presented in Appendix A.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Votrient, as of September 3, 2009.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Votrient, 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, Votrient, 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 Drug Oncology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

1. OSE Review # 2008-177. Proprietary Name Review of Votrient, Lori Cantin. May 6, 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

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis (DMEPA) for review. The list is updated weekly and maintained by DMEPA.

APPENDICES

Appendix A: Proposed Proprietary Names that have never been Marketed		
Proprietary name	**Similarity to Votrient**	**Status**
(b) (4)		

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

/s/

LORI G CANTIN
09/24/2009

DENISE P TOYER
09/25/2009

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:	May 6, 2009
To:	Robert Justice, MD, Director Division of Drug Oncology Products
Thru:	Kristina Arnwine, Pharm.D., Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
From:	Lori Cantin, R.Ph., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name:	Votrient (Pazopanib) Tablets, 200 mg and 400 mg
Application Type/Number:	NDA 22-465
Applicant:	GlaxoSmithKline
OSE RCM #:	2009-177

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CONTENTS

EXECUTIVE SUMMARY

The Applicant has proposed the proprietary name, Votrient, for Pazopanib Tablets, 200 mg and 400 mg. The proposed product is a tyrosine kinase inhibitor indicated for the treatment of advanced renal cell carcinoma. Both DDMAC and the review division did not have any concerns with the proposed name. We analyzed a total of 61 names to determine if they could be confused with Votrient. Our FMEA found that the proposed name, Votrient, is not vulnerable to name confusion that could lead to medication errors with any currently marketed products. Thus, DMEPA has no objection to the use of the proprietary name, Votrient, for this product.

However, if any of the approved product characteristics as stated in this review are altered, 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.

1 BACKGROUND

1.1 INTRODUCTION

The Applicant submitted a request for a review of the proposed proprietary name, Votrient, on February 13, 2009, for the proposed product, Pazopanib Tablets, 200 mg and 400 mg. The proposed name, Votrient, is evaluated to determine if the name could potentially be confused with other proprietary or established drug names.

1.2 REGULATORY HISTORY

This review is in response to a request to the Applicant's request for a proprietary name review of the proposed proprietary name, Votrient. The New Drug Application (NDA 22-465) for this product was submitted on December 19, 2008. The Applicant also submitted container labels, carton, and package insert labeling for review. The labels and labeling for the proposed product will be reviewed under separate cover (OSE Review #2009-310).

1.3 PRODUCT INFORMATION

Votrient (Pazopanib) is a tyrosine kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma. The recommended dose is 800 mg orally once daily without food (at least 1 hour before or 2 hours after a meal). Dosage modification should be made in 200 mg increments in as stepwise fashion based on individual patient tolerability. The dose of Votrient should not exceed 800 mg per day. A dose of 400 mg orally once daily is recommended in patients receiving a strong CYP3A4 inhibitor concomitantly. The dose of Votrient may also need to be reduced or discontinued for persistent or severe hypertension. Votrient will be available in gray 200 mg and yellow 400 mg modified capsule-shaped, film-coated tablets. The 200 mg tablets will be supplied in bottles of 30 tablets and 90 tablets, and the 400 mg tablets will be supplied in bottles of 30 tablets and 60 tablets.

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis staff conducting a proprietary name risk assessment (see section 2.1). The primary focus for the assessment is to identify and remedy potential sources of medication errors prior to drug approval.

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. [1]

2.1 PROPRIETARY NAME RISK ASSESSMENT

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

For the proprietary name, Votrient, the Division of Medication Error Prevention and Analysis staff searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see sections 2.1.1) and held a CDER Expert Panel Discussion (EPD) to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). We also conduct internal FDA prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see 2.1.3).

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 2.1.4). 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 look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. We use the clinical expertise of the DMEPA staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics 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, we consider 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 08/08/2008.

[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 'V' 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.[1,2]

To identify drug names that may look similar to Votrient, 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 (8 letters), upstrokes (three, capital letter 'V' and lower case letters 't' and 't'), down strokes (none), cross-strokes (two, lower case letters 't' and 't'), and dotted letters (one, lower case letter 'i'). Additionally, several letters in Votrient may be vulnerable to ambiguity when scripted, including the capital letter 'V' may appear as 'L', and 'N'; lower case 'o' may resemble a lower case 'a', 'e', or 'u'; lower case 't' may appear as lower case 'f' or 'l'; lower case 'r' may appear as lower case 'i' or 'n'; lower case 'i' may appear as lower case 'e'; lower case letter 'e' may appear as a lower case letter 'a' or 'i'; lower case 'n' may appear as lower case 'r' or 'v'; and lower case 't' may appear as lower case 'f' or 'l'. As such, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Votrient.

When searching to identify potential names that may sound similar to Votrient, the DMEPA staff search for names with similar number of syllables (3), stresses (VO-tri-ent, vo-TRI-ent, vo-tri-ENT) and placement of vowel and consonant sounds. In addition, several letters in Votrient may be subject to interpretation when spoken; including the letter 'V' which may be interpreted as 'B' or 'F', or the letter string 'HO', with the 'H' being silent; the letter 'f' may be interpreted as 'ph', 'and the letter 't' may be interpreted as 'd'. The Applicant's intended pronunciation of the proprietary name was also taken into consideration (Voh-tree-ent), as it was included in the external proprietary name assessment.

The DMEPA staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Votrient), the established name (Pazopanib), proposed indication (advanced renal cell carcinoma), strength (200 mg and 400 mg), dose (800 mg), frequency of administration (once daily), route of administration (oral), and dosage form of the product (tablet). 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 name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names 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 provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

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

[2] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artifical Inteligence 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 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the DMEPA staff uses 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 reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Votrient. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group 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 Votrient 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 122 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 Votrient in handwriting and verbal communication of the name, one inpatient and one outpatient medication orders were written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 122 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 the DMEPA staff.

Figure 1. Votrient Study (conducted on January 30, 2009)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: Votrient 400mg 2 tabs po daily	
Outpatient Medication Order: Votrient 400mg #60 Take 2 tablets by mouth daily	Votrient 400 mg #60 Take 2 tablets by mouth daily.

2.1.3 External Proprietary Name Risk Assessment

For this product, the Applicant submitted an external evaluation of the proposed proprietary name, Votrient. 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 Drug Oncology 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 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode 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.[1] 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 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 Votrient 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 Votrient 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 possesses 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.

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

DMEPA will object to the use of a proposed proprietary name when one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. 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. DMEPA identifies 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 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 the use of 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 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, which 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 approving the error-prone proprietary name. Moreover, even after a Sponsor 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 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 would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The search retrieved thirty (30) names as having some similarity to Votrient.

Nineteen (19) of the 30 names were thought to look like Votrient. These include: Volmax, Voluven, Vitrasert, Nutrient, Lotrisone, NitroMist, Vanacet, (b) (4) Vitron-C, Vytone, Sotret, Atrovent, Nebupent, Votamed, Votaxil, Striant, Valergen, Vitrase, and Vatrem.

Four (4) names were thought to sound similar to Votrient. These include: Triant-HC, Valproate, Viravan, and Valerian.

Seven (7) names were thought to look and sound similar to Votrient. These include: Voltaren, Votrace, Votrient, Lotensin, Lotrimin, Lotronex, and Vytorin.

The proposed proprietary name, Votrient, does not contain a USAN stem as of the last date searched, March 27, 2009.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by Division of Medication Error Prevention and Analysis staff (see section 3.1.1), and noted no additional names thought to have orthographic or phonetic similarity to Votrient. One EPD panelist suggested that the safety evaluator search 'Z' names for potential names that may look like Votrient. A search of 'Z' names was conducted as part of the independent safety evaluator's search; however, no additional names with orthographic similarity to Votrient were identified.

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 23 responses were evaluated in the prescription analysis studies. None of the responses overlapped with any existing or proposed drug names. Fifty-seven percent (57%) of the participants (n=13) interpreted the name correctly as "Votrient". All the remaining responses misinterpreted the drug name. Five (n=5) responses misinterpreted the name as 'Vatrient', while two (n=2) respondents misinterpreted the name as 'Natrient'. The remaining three (n=3) participants misinterpreted the name as 'Votricent', 'Voltrient', and 'Votrean'. 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, (b) (4) identified and evaluated a total of thirty-eight drug names thought to have some potential for confusion with the name Votrient. Nine of the thirty-eight names were previously identified in our staff searches and include Atrovent, Lotrimin, Lotrisone, Sotret, Striant, Triant-HC, Vitrasert, Voltaren, and Vytorin.

Twenty-nine (29) names were not previously identified by DMEPA. DSI's assessment determined that the following names have similar sound and/or appearance to Votrient: Buprenex, Combivent, Ecotrin, Fetrin, Foltrate, Foltrin, Loestrin 1.5/30-21, Loestrin 1/20-21, Motrin, Motrin IB, Nutrinate, Photofrin, Trental, Tri-Vent HC, Trinate, Trionate, Ultravate, Valium, Valproic Acid, Valtrex, Ventolin, Verapamil, Viagra, Volumen, Vontrol, Vorinostat, Vynase, Zorprin, and Zostrix.

The results of the proposed name risk assessment conducted by Drug Safety Institute, Inc. (DSI) support the use of 'Votrient' as a proprietary name for this drug product.

3.1.5 Comments from the Division of Drug Oncology Products

In response to the OSE March 9th, 2009, e-mail, the Division of Drug Oncology Products did not forward any comments and or concerns on the proposed proprietary name at the initial phase of the name review.

DMEPA notified the Division of Drug Oncology Products via e-mail that we had no objections to the proposed proprietary name, Votrient, on April 28, 2009. This email detailed DMEPA's concern regarding the potential for name confusion with (b) (4), a name currently within the Agency. It was noted that the name, (b) (4), has been already been found unacceptable twice and it is highly unlikely that this name will ever be approved. Therefore, DMEPA has no objection to the name, Votrient, at this time. Per e-mail correspondence from the Division of Drug Oncology Products on May 6, 2009, they indicated they concur with our assessment of the proposed proprietary name, Votrient.

3.1.6 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator identified two additional names thought to look and/or sound similar to Votrient and represent a potential source of drug name confusion The two names are 'Velivet' and 'Viadent'. As such, a total of sixty-one (61) names were analyzed to determine if the drug names could be confused with Votrient, and if the drug name confusion would likely result in a medication error.

Thirty names (30) were not analyzed further for the following reasons:

- Twenty-nine (29) names do not have convincing orthographic and/or phonetic similarity and should not result in medication errors with Votrient (see Appendix C).
- One (1) name, Votrient, is the name trademarked by the Applicant of this NDA for the drug product that is the subject of this review.

Failure mode and effect analysis was then applied to determine if the proposed name, Votrient, could potentially be confused with any of the remaining thirty-one (31) names and lead to medication errors. This analysis determined that the name similarity between Votrient and the identified names was unlikely to result in medication errors for thirty (30) of the thirty-one (31) products identified for the reasons presented in Appendices D through I.

FMEA determined that the one (1) remaining name, (b) (4), a pending name within the Agency, was vulnerable to confusion and could result in medication errors with Votrient in the clinical setting due to orthographic, phonetic and product characteristic similarities to Votrient. These concerns are further detailed in section 4.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

DMEPA analyzed a total of sixty-one (61) names for their potential similarity to the proposed name, Votrient. The findings of the FMEA indicate that the proposed name, Votrient, has orthographic and phonetic similarity to, and overlapping product characteristics with, (b) (4), which makes it vulnerable to confusion that could lead to medication error.

As part of our name risk assessment, we considered all of the orthographic and phonetic characteristics of the names, and the product characteristics of the proposed products, Votrient and (b) (4)

Orthographically, Votrient looks like (b) (4) (b) (4)

(b) (4)

(b) (4) Therefore, we have no objection to the name, Votrient, at this time.

5 CONCLUSIONS & RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Votrient, is not vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Votrient, for this product at this time.

Additionally, DDMAC does not object to the proposed name, Votrient, from a promotional perspective. The results of the proposed name risk assessment conducted by (b) (4) also support the use of 'Votrient' as a proprietary name for this drug product.

However, if any of the approved product characteristics as stated in this review are altered, 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

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 Sandra Griffith, OSE Project Manager, at 301-796-2445.

5.2 COMMENTS TO THE APPLICANT

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

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

If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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 Errors Prevention and Analysis proprietary name consultation requests

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

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

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name 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)

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

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

Provides information regarding patent and trademarks.

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

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.

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

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

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

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)

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.

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

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. 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. The Division of Medication Error Prevention and Analysis also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The medication error staff also 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* 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 (i.e. "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 compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, we will consider the Sponsor's intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, we also consider a variety of pronunciations that could occur in the English language.

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

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	**Attributes examined to identify similar drug names**	**Potential Effects**
Look-alike	**Similar spelling**	**Identical prefix** **Identical infix** **Identical suffix** **Length of the name** **Overlapping product characteristics**	• **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**	• **Names may look similar when scripted, and lead to drug name confusion in written communication**

		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:

FDA Prescription Study Responses

Inpatient Medication Order		**Outpatient Medication Order**	**Voice Prescription**
Voltrient	Votrient	Vatrient	Votrean
Votrient	Votrient	Vatrient	
Votrient	Votrient	Natrient	
Votrient	Votrient	Vatrient	
Votrient	Votricent	Natrient	
Votrient	Votrient	Vatrient	
Votrient	Votrient	Vatrient	
Votrient			

Appendix C: Proprietary names lacking convincing orthographic and/or phonetic similarities with Votrient.		
Proprietary Name	**Similarity to Votrient [Look, Sound, or NS (not specified)]**	**Source (b) (4) or DMEPA)**
Vytone	Look	DMEPA
Voluven	Look	DMEPA
Sotret	Look	DMEPA
Valergen	Look	DMEPA
Viravan	Sound	DMEPA
Valerian	Sound	DMEPA
Zostrix	Look	(b) (4)
Zorprin	Look	
Vyvanse	NS	
Vorinostat	Look	
Volumen	NS	
Viagra	NS	
Verapamil	NS	
Valproic Acid	NS	
Valium	NS	
Ultravate	NS	
Trionate	Look	
Trinate	Look	
Tri-Vent HC	Sound	
Trental	Sound	
Photofrin	Look	

Appendix C: Proprietary names lacking convincing orthographic and/or phonetic similarities with Votrient.		
Proprietary Name	**Similarity to Votrient [Look, Sound, or NS (not specified)]**	**Source (b) (4) or DMEPA)**
Motrin IB	Look	(b) (4)
Loestrin 1/20-21	Look	
Loestrin 1.5/30-21	Look	
Foltrate	Look	
Fetrin	Look	
Ecotrin	Look	
Combivent	NS	
Buprenex	Sound	

Appendix D: Proprietary names identified only in Foreign Countries.		
Proprietary name	**Similarity to Votrient**	**Country**
Votrace (Calcitriol)	LA	Greece
Vatrem (Piroxicam)	LA	Mexico
Votaxil (Diclofenac Sodium)	LA	Venezuela
Votamed (Diclofenac Sodium)	LA	Thailand

Appendix E: Nonprescription product name or general term not likely to be written as a prescription

Proprietary Name	Similarity to Votrient	Description
Viadent	LA	Toothpaste (Original and Advanced Care) and Mouthrinse
Nutrient	LA/SA	Not a specific drug product; general term for a substance or ingredient that provides nourishment

Appendix F: Proprietary Names of Drug Products that are no Longer Marketed, are Discontinued, or are Withdrawn by the FDA Commissioner, and there are no Generic Equivalent Products Available

Proprietary name	**Similarity to Votrient**	**Status**
Vontrol (Diphenidol Hydrochloride)	LA	Withdrawn by Commissioner: 6/4/2004 NDA 16-034 (Injection) NDA 16-035 (Suspension) NDA 16-036 (Suppository) Withdrawn by Commissioner: 3/13/2009 NDA 16-033 (Tablets)

Appendix G: Drug Products with no Numerical Overlap in Strength or Dose

Votrient (Pazopanib)		200 mg and 300 mg	Usual dose: 200 mg, 400 mg, 600 mg, or 800 mg once daily
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Vitrasert (Ganciclovir)	LA	4.5 mg	1 implant into each affected eye; remove or replace after 5 to 8 months
Lotrisone (Clotrimazole and Betamethasone Dipropionate)	LA	1%/0.5%	Apply topically to affected areas of skin twice daily
NitroMist (Nitroglycerin)	LA	0.4 mg per spray	(1) 1 or 2 sprays on or under the tongue at the onset of an anginal attack; May repeat every 5 minutes to a max of 3 doses. (2) Prophylactically, 1or 2 sprays 5 or 10 minutes prior to activity that may cause angina
Vanacet (acetaminophen and hydrocodone bitartrate)	LA	500 mg/5 mg	1 or 2 tablets orally every 4 to 6 hours; max of 8 tablets per day (Note: Off market per Clin Pharm; not found in Red Book)
Vitron-C (Ascorbic Acid/Ferrous Fumarate)	LA	125 mg/66 mg	1 or 2 tablets orally 1 to 3 times per day
Atrovent (Ipratropium Bromide)	LA/SA	Inhalation aerosol: 18 mcg/actuation Nasal Spray: 0.06 % (42 mcg per spray)	2 oral inhalations 4 times a day; 2 sprays intranasally 3 or 4 times a day
Nebupent (Pentamidine Isethionate)	LA	300 mg/vial	Inhale via Respirgard II nebulizer at a rate of 5 to 7 liters per minute (approx. 30 to 45 minutes), once every 4 weeks
Striant (Testosterone)	LA	30 mg	One tablet twice daily, buccally

Appendix G: Drug Products with no Numerical Overlap in Strength or Dose

Votrient (Pazopanib)		200 mg and 400 mg	Usual dose: 200 mg, 400 mg, 600 mg, or 800 mg once daily
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Triant-HC (Hydrocodone, Chlorpheniramine, Phenylephrine)	SA	1.67 mg/2 mg/5 mg per 5 mL	½, 1 or 2 teaspoonsful orally every 4 to 6 hours; max of 4 doses per day
Voltaren (Diclofenac Sodium)	LA	0.1% ophthalmic solution Delayed-release tablet: 25 mg, 50 mg, and 75 mg 1% topical gel	1 drop to affected eye, 4 times daily beginning 24 hrs pre-op and continuing x 2 weeks; or 1 to 2 drops within 15 minutes of surgery and continue 4 times/day x 3 days 100 mg to 200 mg per day, orally, divided twice, three times, or 4 times daily; 2 gm to 4 gm 4 times per day, topically, to joints
Lotrimin (Clotrimazole)	LA/SA	1 %	Apply topically twice daily
Lotronex (Alosetron Hydrochloride)	LA	0.5 mg and 1 mg	0.5 mg to 1 mg orally twice daily
Foltrin (Iron, Vitamin B12, intrinsic factor, Vitamin C, Folic Acid)	SA	110 mg, 15 mcg, 240 mg, 75 mg, 0.5 mg	Likely unapproved, marketed Rx supplement; dose not specified in commonly used references and databases
Velivet (Desogestrel, ethinyl estradiol)	LA	0.1 mg/0.025 mg 0.125 mg/ 0.025 mg 0.15 mg/ 0.025 mg	1 tablet orally once daily
Nutrinate (Rx Multivitamin) "off market" per clinpharm	LA	Multivitamin Chewable Tablet	Likely 1 tablet orally once daily; specific dosing information not specified in commonly used references
Valtrex (Valacyclovir)	LA	500 mg Tablet	1 gm 2 or 3 times a day for 7 or 10 days; 500 mg twice daily for 3 days; 500 mg or 1 gm once daily; 2 gm twice daily for 1 day

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

Product name with potential for confusion	Similarity to Votrient	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics Votrient vs. Potentially Confusing Product Name
Ventolin* (Albuterol Sulfate) *Brand name Solution of inhalation, oral tablets and oral syrup are discontinued, but products are available generically.		Inhalation aerosol: 90 mcg albuterol per actuation Solution for inhalation: 0.083% and 0.5% Oral Tablets: 2 mg and 4 mg Oral Syrup: 2 mg/5 mL	**Inhalation aerosol:** 1 or 2 inhalations every 4 to 6 hours, or 2 inhalations 15 to 30 minutes before exercise. **Solution for inhalation:** 2.5 mg 3 to 4 times a day by nebulization **Oral Tablets and Oral Syrup:** Orally, 2 mg or 4 mg, 3 or 4 times a day; Children age 2-6: 0.1 mg/kg	*Frequency of administration* (once daily vs. 3 or 4 times per day, or every 4 to 6 hours)
Motrin* (Ibuprofen) *Brand name prescription strengths are discontinued, but product is available generically: Nonprescription products may be prescribed as 'Motrin' rather than full brand names (Motrin IB, Children's Motrin, Motrin Junior Strength, etc)		Oral Tablets: 100 mg, 200 mg, 400 mg, 600 mg, 800 mg Oral Chewable Tablets: 50 mg and 100 mg Oral Suspension: 100 mg/5 mL Oral Drops: 40 mg/mL	Adults: Orally, 200 mg, 400 mg, 600 mg, every 4 to 6 hours as needed; 1200 mg to 3200 mg daily (3 or 4 divided doses) Children: 10 mg/kg/dose every 6 to 8 hours	*Frequency of administration* (once daily vs. 3 or 4 times per day, every 4 to 6 hours, or every 6 to 8 hours) *Prescription status* (Rx vs. OTC)

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

[redacted]

Product name with potential for confusion	Similarity to Votrient	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics Votrient vs. Potentially Confusing Product Name
Vitrase (Hyaluronidase)	LA	Solution for injection: 200 units/mL Lyophilized powder for injection: 6200 units/vial	Dose varies: 50 units, 75 units, 100 units, 150 units, 200 units, 300 units; no specific frequency for this product	*Dosage Form* (Oral Tablet vs. Injection) *Route of Administration* (Oral vs. Subcutaneous, Hypodermic) *Frequency of Administration* (Once daily vs. varied) Vitrase would not be prescribed by itself; it is indicated as an adjuvant to increase the absorption and dispersion of other injected drugs; for hypodermoclysis; and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents.
Volmax* (Albuterol Sulfate) *Brand discontinued per OB; Withdrawn (4/4/05); generics available: ANDA 76-130 and ANDA 78-092	LA	Extended-release Tablets: 4 mg and 8 mg	4 mg to 8 mg orally every 12 hours	*Frequency of Administration* (Once daily vs. every 12 hours) *Strength* (200 mg and 400 mg vs. 4 mg and 8mg)
Valproate (Valproate Sodium)	LA	100 mg/mL, 5 mL vial	10 to 60 mg/kg/day intravenously as a 60-minute infusion; doses greater than 250 mg per day should be given in divided doses (2 to 6 times per day)	*Dosage Form* (Oral Tablet vs. Injection) *Route of Administration* (Oral vs. Intravenous)

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

[redacted]

Product name with potential for confusion	Similarity to Votrient	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics Votrient vs. Potentially Confusing Product Name
Voltaren (Diclofenac Sodium)	LA	0.1% ophthalmic solution Delayed-release tablet: 25 mg, 50 mg, and 75 mg 1% topical gel	1 drop to affected eye, 4 times daily beginning 24 hrs pre-op and continuing x 2 weeks; or 1 to 2 drops within 15 minutes of surgery and continue 4 times/day x 3 days 100 mg to 200 mg per day, orally, divided twice, three times, or 4 times daily 2 gm to 4 gm 4 times per day, topically, to joints	*Dose** (200 mg, 400 mg, 600 mg, 800 mg vs. 25 mg, 50 mg, 75 mg) *Frequency of Administration* (Once daily vs. twice daily, three times daily, or four times daily) *Only total daily dose of Voltaren 200 mg per day overlaps with the 200 mg strength and dose of Votrient.

Appendix I: Potential for name confusion with overlap in dose or strength and frequency but with phonetic, orthographic, and/or product characteristic differences

Failure Mode (Name confusion)	Causes (could be multiple)	Effects
Lotensin (Benazepril) 5 mg, 10 mg, 20 mg, 40 mg Tablets 10 mg to 80 mg per day, divided once or twice daily	**Orthographic Similarity:** First letter similarity ('L' looks like 'V') Names are the same length (8 letters) Prefix looks similar when scripted ('Lot' vs. 'Vot') Both names contain 1 dotted letter ('i') **Phonetic Similarity:** The prefix of Votrient ('Vot') sounds like the prefix of Lotensin ('Lot') **Similar Product Characteristics:** Numerical similarity in strength (20 mg vs. 200 mg and 40 mg vs. 400 mg); similarity is exacerbated if a terminal zero (e.g. 20.0) is included with Lotensin 20 mg Same frequency of administration (Once daily) Same dosage form (Oral Tablets)	Orthographic and phonetic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. *Rationale:* **Orthographic Differences:** Votrient has three upstrokes ('V', 't', and 't') while Lotensin has two upstrokes ('L' and 't'). Additionally, the last letter of Votrient is an upstroke ('t') while the last letter of Lotensin is not an upstroke, which helps to differentiate these two names when scripted Votrient contains 2 cross-strokes ('t' and 't') while Lotensin contains only 1 cross-stroke ('t') The infix and suffix of Votrient (tri-ent) do not look like the infix and suffix of Lotensin (ten-sin) when scripted. **Phonetic Differences:** The infix and suffix of Votrient (tri-ent) do not sound similar to the infix and suffix of Lotensin (ten-sin) **Differences in Product Characteristics:** There is a similarity in doses (e.g., 200 mg or 400 mg vs. 20 mg or 40 mg), but not a complete overlap. This similarity would be exacerbated by the addition of a terminal zero to the Lotensin dose (e.g., 20.0 mg), however, usual practice would not typically involve the inclusion of trailing zeros, though medication errors have been linked to this dangerous habit. Numerous campaigns (JCAHO, ISMP, FDA) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.

Appendix I: Potential for name confusion with overlap in dose or strength and frequency but with phonetic, orthographic, and/or product characteristic differences

Failure Mode (Name confusion)	Causes (could be multiple)	Effects
Vytorin (Ezetimibe and Simvastatin) Tablets: 10 mg/10 mg 10 mg/20 mg 10 mg/40 mg 10 mg/80 mg 10 mg/10 mg to 10 mg/80 mg once daily	**Orthographic Similarity:** Same first letter ('V') Names are similar length (8 letters vs. 7 letters) Both names contain the upstroke 't' in the third position Both names contain one dotted letter ('i') **Phonetic Similarity:** When spoken, the prefix 'Vot' may sound like the name 'Vyt', especially if the 'y' is not clearly enunciated **Similar Product Characteristics:** Numerical similarity in strength and dose of simvastatin component of Vytorin (200 mg vs. 10 mg/20 mg, 10 mg/40 mg, and 10 mg/80 mg) if the doses of both ingredients of Vytorin are not specified when prescribed. Same frequency of administration (Once daily) Same dosage form (Oral Tablets)	Orthographic and phonetic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. *Rationale:* **Orthographic Differences:** Votrient has three upstrokes ('V', 't', and 't') while Vytorin has two upstrokes ('V' and 't'). Additionally, the last letter of Votrient is an upstroke ('t') while the last letter of Vytorin is not an upstroke, which helps to differentiate these two names when scripted Votrient has no downstrokes while Vytorin has 1 downstroke ('y') Votrient contains 2 cross-strokes ('t' and 't') while Vytorin contains only 1 cross-stroke ('t') **Phonetic Differences:** The last 4 letters in the name Votrient 'ient' do not sound like the last 4 letters in the name Vytorin 'orin' when spoken. **Differences in Product Characteristics:** When prescribed, the doses of both ingredients of Vytorin will typically be specified, which will differentiate the dose of Vytorin from the dose of Votrient. Additionally, if only the second ingredient (simvastatin) is specified, there is not a complete overlap in dose unless a trailing zero is used (e.g. 200 mg vs. 20.0 mg), and usual practice would not typically involve the inclusion of trailing zeros, though medication errors have been linked to this dangerous habit. Numerous campaigns (JCAHO, ISMP, FDA) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.

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