

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**125377Orig1s000**

**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: March 18, 2011

Application Type/Number: BLA 125377

Through: Todd Bridges, RPh, Acting Deputy Director *Todd Bridges 3/18/11*  
Carol Holquist, RPh, Director *Carol Holquist 3/18/11*  
Division of Medication Error Prevention and Analysis (DMEPA)

From: Jibril Abdus-Samad, PharmD, Safety Evaluator *Todd Bridges for JA 3/18/11*  
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Yervoy (Ipilimumab) Injection,  
50 mg/10 mL, 200 mg/40 mL

Applicant/Applicant: Bristol-Myers Squibb Company

OSE RCM #: 2010-2730

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

## **1 INTRODUCTION**

This re-assessment of the proprietary name, Yervoy, responds to the anticipated approval of BLA 125377 within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Yervoy, acceptable in OSE Review 2010-1477, dated September 27, 2010.

## **2 METHODS**

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see Section 5) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the completion of the previous OSE proprietary name review. We use the same search criteria outlined in OSE Review #2010-1477, for the proposed proprietary name, Yervoy. 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)<sup>1</sup> of the proposed proprietary name, and focuses on the avoidance of medication errors.

## **3 RESULTS**

The safety evaluator searches of the databases listed in Section 5 identified two additional names, Toviaz and (b)(4)<sup>\*\*\*</sup>, thought to look similar to Yervoy and represent a potential source of drug name confusion (see Appendices A and B). Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of March 16, 2011.

## **4 CONCLUSIONS AND RECOMMENDATIONS**

The Proprietary Name Risk Assessment indicates that the proposed name, Yervoy, 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 proposed proprietary name, Yervoy, 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, DBOP should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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<sup>1</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

<sup>\*\*\*</sup> This document contains proprietary and confidential information that should not be released to the public.

## 5 REFERENCES

1. Abdus-Samad, J. OSE Review #2010-1477: Proprietary Name Review for Yervoy. September 27, 2010.
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. ***USAN Stems*** (<http://www.ama-assn.org/ama/pub/category/4782.html>)  
USAN Stems List contains all the recognized USAN stems.
4. ***Division of Medication Error Prevention and Analysis proprietary name 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.

**Appendix A:** Proprietary names no longer active

Proprietary Name	Similarity to Yervoy	Comments
(b) (4)	Look	NDA 22211 approved as with proprietary name <i>Zirgan</i>

**Appendix B:** Names with orthographic differences and different product characteristics that minimize the risk of medication error.

Product name with potential for confusion	Similarity to Yervoy	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
<b>Yervoy (Ipilimumab)</b>		<b>50 mg/10 mL injection, 200 mg/40 mL injection</b>	<b>Inject 3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of 4 doses.</b>  <b>Dose ranges from 135 mg to 350 mg for 45 kg to 115 kg patients</b>	
Toviaz (Fesoterodine Fumarate)	Look	4 mg, 8 mg tablets	Take 1 tablet orally once daily	<b>Orthographic differences:</b> The initial letters, capital letters 'T' and 'Y' are distinct.  <b>Dose:</b> 4 mg, 8 mg (1 tablet) vs. 135 mg to 350 mg for 45 kg to 115 kg patients  <b>Dosage form and route of administration:</b> oral tablets vs. intravenous injection  <b>Frequency of administration:</b> once daily vs. once every 3 weeks

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Department of Health and Human Services  
Public Health Service  
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Office of Surveillance and Epidemiology

Date: September 27, 2010

Application Type/Number: BLA 125377

Through: Todd Bridges, RPh, Team Leader *Carol Holquist for 9/27/2010*  
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Division of Medication Error Prevention and Analysis  
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From: Jibril Abdus-Samad, PharmD, Safety Evaluator *JAS 9/27/2010*  
Division of Medication Error Prevention and Analysis  
(DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Yervoy (Ipilimumab) Injection,  
50 mg/10 mL, 200 mg/40 mL

Applicant/Applicant: Bristol-Myers Squibb Company

OSE RCM #: 2010-1477

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## **EXECUTIVE SUMMARY**

This review summarizes DMEPA's evaluation of the proposed proprietary name, Yervoy for Ipilimumab Injection. Our evaluation identified no concerns from a safety and promotional perspective that would render the name unacceptable. Thus, DMEPA finds the proposed proprietary name, Yervoy, acceptable for this product. The Applicant will be notified by letter.

The proposed proprietary name must be re-evaluated 90 days prior to approval of the BLA. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

## **1 BACKGROUND**

### **1.1 INTRODUCTION**

The Applicant, Bristol Myers Squibb Company, requested an assessment of the proposed proprietary name in a submission dated June 30, 2010.

The Division of Medication Error Prevention and Analysis (DMEPA) assesses a proposed proprietary name regarding its potential for name confusion with other proprietary or established drug names in the usual practice settings. Additionally, DMEPA considers the Division of Drug Marketing, Advertising and Communications' (DDMAC's) promotional assessment of the name.

### **1.2 PRODUCT INFORMATION**

Yervoy is the proposed proprietary name for Ipilimumab Injection. Yervoy has a proposed indication for treatment of advanced melanoma (unresectable Stage III and Stage IV melanoma) in patients who have received prior therapy. The recommended dose is 3 mg/kg administered intravenously over a 90 minute period every 3 weeks for a total of four doses. Yervoy will be supplied as 50 mg/10 mL and 200 mg/40 mL vials and must be refrigerated at 2° C to 8° C (36° F to 46° F).

## **2 METHODS AND MATERIALS**

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, and 2.2 identify information associated with the methodology for the proposed proprietary name, Yervoy.

## 2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘Y’ 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.<sup>1,2</sup>

To identify drug names that may look similar to Yervoy, the DMEPA safety evaluators also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (one, capital letter Y), down strokes (one, lowercase y), cross strokes (none), and dotted (none). Additionally, several letters in Yervoy may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Yervoy.

When searching to identify potential names that may sound similar to Yervoy, the DMEPA safety evaluators search for names with similar number of syllables (two), stresses (YER-voy or yer-VOY), and placement of vowel and consonant sounds. The Applicant’s intended pronunciation (‘yur-voi) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

## 2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication orders and verbal prescription were communicated during the FDA prescription studies.

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

<sup>2</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

**Figure 1. Yervoy Prescription Study (conducted on May 6, 2010 and May 13, 2010)**

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order #1:</u></p> <p><i>Yervoy 250mg IV over 90 minutes</i></p>	<p>Yervoy 250 mg infuse iv over 90 minutes</p>
<p><u>Inpatient Medication Order #2:</u></p> <p><i>Yervoy 250mg IV over 90 minutes</i></p>	

### 3 RESULTS

The names identified from DMEPA’s methods as potential sources for name confusion with Yervoy are listed below.

#### 3.1 DATABASE AND INFORMATION SOURCES

Our searches of database and DMEPA’ information sources yielded a total of nine names as having some similarity to the name Yervoy.

Eight of the names were thought to look like Yervoy. These include: Unasyn, Vermox, Yentreve, (b) (4), Zenpep, Zonvoy, Zosyn, and Zovirax. The remaining name, Yervoy, was thought to look and sound similar to Yervoy.

Additionally, DMEPA safety evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of September 7, 2010.

#### 3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA safety evaluators (see Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Yervoy.

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

#### 3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 40 practitioners responded to the prescription analysis study. The majority of responses for all the studies were incorrect (n=38). There was only one correct response in each of the two inpatient studies. The most common misinterpretation in Inpatient Study #1 was the letter ‘n’ for the letters ‘rv’. In Inpatient Study #2, the most common misinterpretation was the letter ‘v’ for the letter ‘r’. All of the responses in the Verbal

Study were incorrect. The most common misinterpretation in the Verbal Study was the letters 'Ur' for the letters 'Yer'. One response in Inpatient Study #2, Ferring, was similar to the currently marketed product, Femring. Additionally, another response in Inpatient Study #2, Ferrous, was similar to currently marketed products that contain the root word Ferrous. These two names, Femring and Ferrous, are evaluated in the Section 4.2 safety evaluation.

### **3.4 COMMENTS FROM THE DIVISION OF BIOLOGIC ONCOLOGY PRODUCTS (DBOP)**

#### ***3.4.1 Initial Phase of Review***

In response to an April 23, 2010 OSE e-mail, the Division of Biologic Oncology Products (DBOP) indicated they had no particular concerns from a promotional perspective at the initial phase of the name review.

#### ***3.4.2 Midpoint of Review***

DMEPA notified DBOP via e-mail that we had no concerns with the proposed proprietary name, Yervoy, on September 13, 2010. Per e-mail correspondence from DBOP on September 21, 2010, they noted no concerns with the proposed proprietary name, Yervoy.

### **3.5 SAFETY EVALUATOR RISK ASSESSMENT**

Independent searches by the primary DMEPA safety evaluator resulted in the identification of four additional names which were thought to look or sound similar to Yervoy and represent a potential source of drug name confusion. Three names (Varivax, Xanax, and Zomig) were identified as having look-alike similarities. The remaining name, Eurax, was identified as having sound-alike similarities.

Thus, we identified in total, 15 names as having similarity to the proposed name.

## **4 DISCUSSION**

This proposed name, Yervoy, was evaluated from a safety and promotional perspective. Furthermore, input from pertinent disciplines involved with the review of this application was considered accordingly.

### **4.1 PROMOTIONAL ASSESSMENT**

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and the DBOP concurred with the findings of DDMAC's promotional assessment of the proposed proprietary name.

### **4.2 SAFETY ASSESSMENT**

DMEPA identified 15 names for their potential similarity to the proposed name, Yervoy. No other aspects of the name were determined to pose a different source for potential confusion with the name.

Five of the 15 names were eliminated for the reasons described in Appendices D and E. Appendix D lists one proprietary name which lacks sufficient orthographic similarity with Yervoy to result in confusion. Appendix E describes two proprietary names for products that are inactive. Additionally, the name, Ferrous, is the first portion of the name for many products such as Ferrous Fumarate, Ferrous Sulfate, and Ferrous Gluconate. Because the second portion of the name is required for identification and Ferrous is not a complete name of a product, it was eliminated from further analysis. Furthermore, the name, Yervoy, was identified in our database search and is actually the name for this product under review. Since the trademark is licensed to the Applicant, it was eliminated from further analysis.

Failure mode and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the remaining 10 names and lead to medication errors. This analysis determined that the name similarity between Yervoy and all of the 10 identified names was unlikely to result in medication error for the reasons presented in Appendices E through F.

## **5 CONCLUSIONS AND RECOMMENDATIONS**

We have completed our review of the proposed proprietary name, Yervoy, and it is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis has no objections to the proprietary name, Yervoy, at this time. The Applicant will be notified via letter.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

If you have further questions or need clarifications, please contact Sue Kang, project manager, at 301-796-4216.

### **5.1 COMMENTS TO THE APPLICANT**

We completed our review of the proposed proprietary name, Yervoy, and concluded that it is acceptable. The proposed proprietary name will be re-reviewed 90 days before approval of the BLA.

If any of the proposed product characteristics as stated in your June 30, 2010 submission are altered, the proprietary name should be resubmitted for review.

## 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; it contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. ***FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]***

DARRTS is a government database used to organize Applicant and Applicant submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

**9. *Clinical Pharmacology Online* ([www.clinicalpharmacology-ip.com](http://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](http://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](http://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](http://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/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)**

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](http://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:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>3</sup>

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>4</sup> DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

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

<sup>4</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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.<sup>5</sup> DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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<sup>5</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

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

<b>Type of similarity</b>	<b>Considerations when searching the databases</b>		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>
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	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

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

## **1. Database and Information Sources**

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

## **2. CDER Expert Panel Discussion**

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

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

## **3. 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 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify 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.

#### 4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division 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. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or OGD 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 OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

#### 5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>6</sup> When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

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<sup>6</sup> Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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

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

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

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

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to

recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

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

with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

**Appendix B:** Potential orthographic or phonetic misinterpretation of the letters in the name Yervoy

<b>Letters in Name, Yervoy</b>	<b>Scripted may appear as</b>	<b>Spoken may be interpreted as</b>
Capital 'Y'	G, U, V, X, Y, Z, f, p	any vowel
lowercase 'e'	a, c, i, l	any vowel
lowercase 'r'	c, n, v	wr
lowercase 'v'	r, u,	b, v
lowercase 'o'	a, e, u,	any vowel
lowercase 'y'	g, x	any vowel

**Appendix C: FDA Prescription Study Responses (May 5, 2010 and May 13, 2010)**

<b>Inpatient Medication Order # 1</b>	<b>Inpatient Medication Order #2</b>	<b>Voice Prescription</b>
Femoy	Ferring	Urevoi
Yenay	Ferrous	Urovoid
Yenay	Yemroy	Urvoid
Yenoy	Yerring	Urvoid
Yenoy	Yerroy	Urvoit
Yenoy	yerroy	Yearvoit
Yenoy	Yerroy	Yourvoy
Yenoy	Yerroy	Yurvoit
Yenoy	Yerroy	Zervoid
Yenoy	Yerroy	
Yerroy	Yerroy	
Yervoy	Yerroy	
	Yervoy	
	Yevroy	
	Yevvoy	
	Yevvoy (if that's v v it will be typed as a "w")	
	Yevvoy or Yenvoy	
	Yevvoy or Yevray	
	Yevvuy	

**Appendix D:** Proprietary Name lacking significant orthographic similarities

<b>Proprietary Name</b>	<b>Similarity to Yervoy</b>	<b>Source</b>
Yentreve	Look	EPD

**Appendix E:** Proprietary names no longer active

<b>Proprietary Name</b>	<b>Similarity to Yervoy</b>	<b>Comments</b>
(b) (4)	Look	NDA 022210 approved on August 27, 2009, with proprietary name <i>Zenpep</i>
Zonvoy	Look	Identified in USPTO as trademark of GlaxoSmithKline however not identified in Drug Information Databases as currently marketed product

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

**Appendix F:** Products with different product characteristics that minimize the risk of medication error

Product name with potential for confusion	Similarity to Yervoy	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
Yervoy (Ipilimumab)		50 mg/10mL injection, 200 mg/40 mL injection	Inject 3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of 4 doses.  Dose ranges from 135 mg to 350 mg for 45 kg to 115 kg patients	
Unasyn (Ampicillin and Sulbactam)	Look	1.5 g, 3 g, for injection  15 g for injection (bulk vial)	Inject 1.5 g to 3 g intravenously or intramuscularly every 6 hours	<b>Dose:</b> 1.5 g or 3 g vs. 135 mg to 350 mg  <b>Orthographic differences:</b> Unasyn contains a letter (lowercase 'n') after the downstroke letter 'y'.  <b>Frequency of Administration:</b> every 6 hours vs. every 3 weeks  Medication order for chemotherapeutic agents are likely to have total volume for the solution and rate of infusion such as Yervoy 225 mg in 100 mL 0.9% Sodium chloride intravenous over 90 minutes
Vermox (Mebendazole)	Look	100 mg tablet	Take 1 tablet orally twice daily for 3 days  Take 1 tablet once as a single dose.	<b>Dose:</b> 100 mg vs. 135 mg to 350 mg  <b>Dosage form and route of administration:</b> oral tablets vs. intravenous injection  <b>Frequency of Administration:</b> 2 times daily or single dose vs. every 3 weeks
Zenpep (Lipase, Protease, and Amylase)	Look	5,000 USP units, 10,000 USP units, 15,000 USP units, 20,000 USP units, delayed release capsules	Children 4 years to Adults: 500 to 2,500 lipase units/kg per meal or (less than or equal to 10,000 lipase units/kg/day)  Children 12 months to younger than 4 years: 1,000 to 2,500 lipase units/kg per meal or (less than or equal to 10,000 lipase units/kg/day)  Infants up to 12 months: 2,000 to 4,000 lipase units/kg per 120 mL of formula	<b>Dose:</b> capsules or units vs. 135 mg to 350 mg  <b>Dosage form and route of administration:</b> oral capsules vs. intravenous injection  <b>Frequency of administration:</b> each meal and snack vs. every 3 weeks

Product name with potential for confusion	Similarity to Yervoy	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
Yervoy (Ipilimumab)		50 mg/10mL injection, 200 mg/40 mL injection	Inject 3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of 4 doses.  Dose ranges from 135 mg to 350 mg for 45 kg to 115 kg patients	
Zovirax (Acyclovir)	Look	200 mg capsule 400 mg, 800 mg tablets 200 mg/5 mL suspension	Chickenpox: 800 mg 4 times daily for 5 days. Genital herpes: 200 mg every 4 hours, 5 times daily for 5 – 10 days 400 mg 2 times daily for up to 12 months Children 2 years and older: 20 mg/kg orally 4 times daily Children over 40 kg: 800 mg 4 times daily for 5 days	<b>Dosage form and route of administration:</b> oral tablets, capsules or solution vs. intravenous infusion  <b>Frequency of Administration:</b> 2 to 5 times daily vs. every 3 weeks
Varivax (Varicella Virus Vaccine Live)	Look	1,350 PFU/0.5 mL	Adults: Inject 0.5 mL subcutaneously then 0.5 mL 4 to 8 weeks later  Children 12 months to 12 years of age: Inject 0.5 mL subcutaneously	<b>Dose:</b> 0.5 mL vs. 135 mg to 350 mg <b>Route of administration:</b> subcutaneous vs. intravenous infusion <b>Frequency of Administration:</b> once then once more 4 to 8 weeks later vs. every 3 weeks  Medication order for chemotherapeutic agents are likely to have total volume for the solution and rate of infusion such as Yervoy 225 mg in 100 mL 0.9% Sodium chloride intravenous over 90 minutes
Xanax (Alprazolam)	Look	0.25 mg, 0.5 mg, 1 mg, 2 mg tablets	Take 1 tablets orally 3 times daily	<b>Dose:</b> 1 tablet (0.25 mg, 0.5 mg, 1 mg, 2 mg) vs. 135 mg to 350 mg <b>Dosage form and route of administration:</b> oral tablets vs. intravenous infusion <b>Frequency of Administration:</b> 3 times daily vs. every 3 weeks

Product name with potential for confusion	Similarity to Yervoy	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
Yervoy (Ipilimumab)		50 mg/10mL injection, 200 mg/40 mL injection	Inject 3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of 4 doses.  Dose ranges from 135 mg to 350 mg for 45 kg to 115 kg patients	
Zomig (Zolmitriptan)	Look	2.5 mg, 5 mg tablets	Take one tablet. May repeat after 2 hours, max 10 mg/24 hours	<b>Dose:</b> 1 tablet (2.5 mg, 5 mg) vs. 135 mg to 350 mg  <b>Dosage form and route of administration:</b> oral tablets vs. intravenous infusion  <b>Frequency of Administration:</b> once, may repeat in 2 hours vs. every 3 weeks
		5 mg nasal solution	One spray intranasally. May repeat after 2 hours, max 10 mg/24 hours	<b>Dose:</b> 5 mg (1 spray) vs. 135 mg to 350 mg  <b>Dosage form and route of administration:</b> nasal spray vs. intravenous infusion  <b>Frequency of Administration:</b> once, may repeat in 2 hours vs. every 3 weeks
Zosyn (Piperacillin Sodium and Tazobactam Sodium)	Look	2.25 g, 3.375 g, 4.5 g for injection  2.25 g, 3.375 g, 4.5 g injection  40.5 g for injection (bulk vial)	Inject 3.375 g to 4.5 g intravenously every 6 hours over 30 minutes  Inject 2.25 g intravenously every 6 to 8 hours over 30 minutes (renal dose adjustment)	<b>Orthographic differences:</b> Zosyn contains an additional letter (lowercase 'n') after the downstroke letter 'y'. Additionally, the downstroke letter 'y' is in the 4 <sup>th</sup> letter position in Zosyn, and in the 6 <sup>th</sup> letter position in Yervoy  <b>Frequency of Administration:</b> every 6 hours vs. every 3 weeks  Medication order for chemotherapeutic agents are likely to have total volume for the solution and rate of infusion such as Yervoy 225 mg in 100 mL 0.9% Sodium chloride intravenous over 90 minutes

Product name with potential for confusion	Similarity to Yervoy	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
Yervoy (Ipilimumab)		50 mg/10mL injection, 200 mg/40 mL injection	Inject 3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of 4 doses.  Dose ranges from 135 mg to 350 mg for 45 kg to 115 kg patients	
Eurax (Crotamiton)	Sound	10% cream 10% lotion	Massage into skin of whole body from chin down. Apply again 24 hours later.	<p><b>Phonetic differences:</b> the last syllables of differ ('-rax' vs. '-voy')</p> <p><b>Dosage form and route of administration:</b> topical cream or lotion vs. intravenous infusion</p> <p><b>Frequency of Administration:</b> once, repeat in 24 hours vs. every 3 weeks</p>
Femring (Estradiol Acetate vaginal ring)	Look	0.05 mg/day, 0.1 mg/day vaginal ring	Insert intravaginally every 3 months	<p><b>Dose:</b> 0.05 mg/day or 0.1 mg /day vs. 135 mg to 350 mg</p> <p><b>Orthographic Differences:</b> Femring appears longer in length</p> <p><b>Dosage form and route of administration:</b> vaginal ring vs. intravenous infusion</p> <p><b>Frequency of Administration:</b> every 3 months vs. every 3 weeks</p>