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RESEARCH**

APPLICATION NUMBER:

203469Orig1s000

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
Office of Medication Error Prevention and Risk Management**

Proprietary Name Review

Date: August 20, 2012

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Drug Name and Strengths: Iclusig (ponatinib) Tablets, 15 mg and 45 mg

Application Type/Number: IND 078375
NDA 203469

Applicant/Sponsor: Ariad

OSE RCM #: 2012-563 and 2012-1924

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Iclusig, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

At the pre NDA meeting was held on February 16, 2012. At that time Division of Medication Error Prevention and Analysis (DMEPA) recommended that a proprietary name be submitted for review. Request for proprietary name review for the IND was submitted on March 2, 2012. The Applicant submitted NDA 203469 on July 30, 2012 and it was granted rolling submission with priority status. On August 10, 2012, the Applicant submitted a request for proprietary name review under the NDA. As a result, this review evaluated the proposed proprietary name, Iclusig, under IND 078375 and NDA 203469.

1.2 PRODUCT INFORMATION

The following product information is provided by the Applicant in the August 10, 2012 proprietary name submission.

- Active Ingredient: Ponatinib
- Indication of Use: Treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) resistant or intolerant to prior tyrosine kinase inhibitor therapy.
- Route of Administration: Oral
- Dosage Form: Tablets
- Strengths: 15 mg, 45 mg
- Dose and Frequency: Start at 45 mg once daily. Decrease to 30 mg to 15 mg in case adverse events occur.
- How Supplied: 15 mg: (b) (4) 60 and 180 tablet count in HDPE bottles. 45 mg: (b) (4) 30 and 90 count in HDPE bottles.
- Storage: Stored at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30° C (59°F to 86°F)
- Container and Closure Systems: Square wide-mouth white high density polyethylene bottles with child resistant closures that incorporate an induction heat seal liner.

2. RESULTS

The following sections provide the information obtained and considered in the evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Hematology Products (DHP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects of the name were considered in the overall safety evaluation.

2.2.1 United States Adopted Names (USAN) SEARCH

On March 21, 2012 the United States Adopted Name (USAN) stem search, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Iclusig, does not have any intended meaning. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Thirty-four practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Out of the 34 participants, 10 participants identified the name as Iclusig while 7 of them identified the name as Ielusig. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, March 21, 2012 e-mail, DHP did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Iclusig. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Iclusig identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from the FDA Prescription Simulation or by Addison Whitney, not identified by DMEPA and require further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, FDA Name Simulation Study, and External Name Study)

Look Similar		Look Similar		Look Similar	
Accolate	Ext	Folcaps	EPD	Invega	Ext
Colace	Ext	(b) (4)***	EPD	Iressa	Ext
(b) (4)***	SE	(b) (4)***	EPD	Isentress	Ext
Enbrel	SE	Iloprost	Ext	Jevity	Ext
Endocet	SE	Inderal	SE	Letairis	SE
Entereg	EPD/Ext	Indocin	EPD/Ext	Levsin	Ext
Enterex	SE	Infasurf	SE	Lustra	Ext
Enulose	Ext	(b) (4)***	SE	Zelnorm	Ext
Eulexin	SE	Intuniv	EPD/Ext	Zolinza	SE
Sound Similar		Sound Similar		Look and Sound Similar	
Eculizumab	Ext	Tasigna	Ext	(b) (4)***	SE
Imatinib	Ext			Invanz	Ext
Increlex	Ext			Istodax	Ext
Ixempra	Ext			Iclusig***	EPD/SE

We determined 36 of the 36 total number of names will not pose a risk for confusion as described in Appendix D and E.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the DHP via e-mail on May 10, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DHP on May 10, 2012, they stated no additional concerns with the proposed proprietary name, Iclusig.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

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

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

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Iclusig, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your March 2, 2012 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days before approval of the NDA. The conclusions upon re-review are subject to change.

4 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. This database also lists the orphan drugs.

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

DARRTS is a government database used to organize Applicant and Sponsor 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. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)

USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online*** (www.clinicalpharmacology-ip.com)

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

9. **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.

10. **Natural Medicines Comprehensive Databases (www.naturaldatabase.com)**

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

11. **Access Medicine (www.accessmedicine.com)**

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. **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.

13. **Red Book (www.thomsonhc.com/home/dispatch)**

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

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

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

15. **Medical Abbreviations (www.medilexicon.com)**

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

16. **CVS/Pharmacy (www.CVS.com)**

This database contains commonly used over the counter products not usually identified in other databases.

17. **Walgreens (www.walgreens.com)**

This database contains commonly used over the counter products not usually identified in other databases.

18. **Rx List (www.rxlist.com)**

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name 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 misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product 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.

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

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.²

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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).

² Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	Considerations when Searching the Databases		
	<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"> 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/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA 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, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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/or 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 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 record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for 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 OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/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 provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

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, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.³ 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 1.2 of this review. The Safety Evaluator then analyzes

³ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

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 or because of some other component of the name. 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.

Moreover, 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 Overall Risk Assessment:

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Sponsor 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/Sponsor. However, the safety concerns set forth in criteria a through e above 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, confusing, or misleading 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 preventable source of medication error that, in many instances, the Agency and/or Sponsor 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. Sponsors have undertaken higher-leverage strategies, such as drug name changes, 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 Sponsors' 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.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Iclusig	Scripted May Appear as	Spoken May Be Interpreted as
I	E, F, J, L, Z	Any vowel
i	a, c, e	Any vowel
c	a, e, i, l, n, o	'k'
l	b, e, i, s	
u	n, w, a, e, i, o, u	Any vowel
s	c, g, n, r	'ce', 'ci'
g	j, q, s	c, k, q
ic	u	
cl	d	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Iclusig Study (Conducted on 3/16/2012)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> <p><i>Iclusig 15mg 1 tablet by mouth daily</i></p> <hr/> <p><u>Outpatient Prescription:</u></p> <p><i>Iclusig 45mg</i> <i>1 tab daily #30</i></p>	<p>Iclusig 45 mg</p> <p>Take 1 orally daily #30</p>

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

84 People Received
Study

34 People Responded

Study Name: Iclusig

	9	10	15	
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
???	1	0	0	1
EYCLUSIQ	0	1	0	1
HYDROCLUSIC	0	1	0	1
ICLURIG	0	0	1	1
ICLUSIC	0	2	0	2
ICLUSICK	0	1	0	1
ICLUSIG	1	3	6	10
ICLUSIK	0	2	0	2
IELURIG	0	0	1	1
IELUSIG	0	0	7	7
ILLEGIBLE	1	0	0	1
JALUSIG	1	0	0	1
JELUSIG	1	0	0	1
JELUSING???	1	0	0	1
JELWAIG	2	0	0	2
JILUSIG	1	0	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to Iclusig	Failure preventions
Accolate	zafirlukast	Orthographic	The pair has sufficient orthographic differences
(b) (4)			
Enulose	lactulose	Orthographic	The pair has sufficient orthographic differences
Iclusig***	ponatinib	Orthographic & Phonetic	Name is the subject of this review
(b) (4)	telbivudine	Orthographic	Product approved as Tyzeka NDA 22011 on 10/25/2006
Ventavis	iloprost*	Orthographic	The pair has sufficient orthographic differences
Gleevec	imatinib*	Phonetic	The pair has sufficient phonetic differences
Increlex	mecasermin	Phonetic	The pair has sufficient phonetic differences
(b) (4)			
Iressa	getfitinib	Orthographic	The pair has sufficient orthographic differences
Isentress	raltegravir	Orthographic	The pair has sufficient orthographic differences
Ixempra Kit	ixabepilone	Phonetic	The pair has sufficient phonetic differences
Jevity	nutritional supplement	Orthographic	The pair has sufficient orthographic differences
Levsin	hyoscyamine	Orthographic	The pair has sufficient orthographic differences

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Lustra	hydroquinone	Orthographic	The pair has sufficient orthographic differences
Tasigna	nilotinib	Phonetic	The pair has sufficient phonetic differences
Zelnorm	tegaserod	Orthographic	The pair has sufficient orthographic differences

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)</p>	<p>Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Colace (docusate) - 50 mg oral capsules - 1 to 6 capsules by mouth daily once or in divided doses</p>	<p>Orthographic Similarities - ‘iclusi’ and ‘colace’ may appear similar when scripted Overlapping Product Characteristics - Route of Administration (oral)</p>	<p>Orthographic Differences - 1 down stroke in the 7th position ‘g’ vs. no down stroke Differing Product Characteristics - Strength (15 mg, 45 mg vs. 50 mg with no overlap)</p>
<p>Established name: eculizumab (Soliris) - 300 mg solution - Induction: 600 mg to 900 mg IV every week x4 weeks then 900 mg to 1200 mg 1 week after - Maintenance: 900 mg to 1200 mg every 2 weeks - Patients < 18 years old: Weight based</p>	<p>Phonetic Similarities - ‘iclusig’ and ‘eculiz’ may sound similar when spoken</p>	<p>Phonetic Differences - eculizumab has extra syllables ‘u’ and ‘mab’ so it sounds longer and different when spoken Differing Product Characteristics - Strength (15 mg, 45 mg vs. 300 mg with no overlap) - Dose (1 tablet vs. individualized dose and weight based dose for pediatric patients) - Frequency of Administration (once daily vs. weekly to every 2 weeks)</p>

Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
(b) (4)		

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Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Enbrel (etanercept) - 40 mg oral tablets - 1 tablet by mouth once daily	Orthographic Similarities - ‘icl’ and ‘enb’ may appear similar when scripted Overlapping Product Characteristics - Dose (1 tablet) - Route of Administration (oral) - Frequency of Administration (once daily) - Dosage Form (tablets)	Orthographic Differences - Down stroke in the 7 th position ‘g’ vs. upstroke in the 6 th position ‘l’ - ‘usi’ and ‘re’ appear different when scripted. Differing Product Characteristics - Strength (15 mg , 45 mg vs. 40 mg with no overlap)
Endocet (oxycodone & acetaminophen) - 5 mg/325 mg, 7.5 mg/ 325mg, 7.5 mg/500 mg, 10 mg/325 mg, 10 mg/ 650mg oral tablets - 1 tablet by mouth every 6 hours as needed	Orthographic Similarities - ‘i’ vs. ‘e’ and ‘cl’ vs. ‘d’ may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Dose (1 tablet) - Route of Administration (oral) - Dosage Form (tablets)	Orthographic Differences - Down stroke in the 7 th position ‘g’ vs. up and cross stroke in the 7 th position ‘t’ Differing Product Characteristics - Strength (15 mg, 45 mg vs. 5 mg/325 mg, 7.5 mg/ 325mg, 7.5 mg/500 mg, 10 mg/325 mg, 10 mg/ 650mg with no overlap) - Frequency of Administration (once daily vs. every 6 hours as needed)

Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Entereg (alvimopan) - 12 mg oral capsules - 1 capsule 30 min to 5 hours prior to surgery followed by 1 capsule by mouth twice daily up to 7 days for max of 15 doses	Orthographic Similarities - ‘clusig’ and ‘entereg’ may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Route of Administration (oral)	Orthographic Differences - No cross stroke vs. 1 cross stroke in the 3 rd position ‘t’ Differing Product Characteristics - Strength (15 mg, 45 mg vs. 12 mg with no overlap)
Enterex (nutritional supplement) - powder for oral suspension - 1 to 3 servings daily as needed	Orthographic Similarities - ‘clusi’ and ‘entere’ may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Route of Administration (oral)	Orthographic Differences - No cross stroke vs. 1 cross stroke in the 3 rd position ‘t’ Differing Product Characteristics - Strength (15 mg , 45 mg vs. single strength with no overlap)
Eulexin (flutamide) - 125 mg oral capsules - 2 capsules by mouth every 8 hours	Orthographic Similarities - ‘clusi’ and ‘eulexi’ may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Route of Administration (oral)	Orthographic Differences - Down stroke in the 7 th position ‘g’ vs. no down stroke ‘n’ Differing Product Characteristics - Strength (15 mg, 45 mg vs. 125 mg with no overlap)

Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Folcaps (vitamin B6, folic acid, cyanocobalamin) - 25 mg/2.2 mg/ 500 µg oral tablets - 1 tablet by mouth once daily	Orthographic Similarities - 'Iclus' and 'Folca' may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Dose (1 tablet) - Route of Administration (oral) - Frequency of Administration (once daily) - Dosage Form (tablets)	Orthographic Differences - 'ig' and 'ps' appear different when scripted due to the position of the down strokes (7 th vs. 6 th position) Differing Product Characteristics - Strength (15 mg, 45 mg vs. single strength with no overlap)

(b) (4)

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Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Inderal (propranolol) - 10 mg, 20 mg, 40 mg, 60 mg, 80 mg oral tablets - 1 tablet by mouth 2 to 4 times daily up to 640 mg/day	Orthographic Similarities - 'Iclusi' and 'Indera' may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Dose (1 tablet) - Route of Administration (oral) - Dosage Form (tablets)	Orthographic Differences - Down stroke in the 7 th position 'g' vs. upstroke in the 7 th position 'l' Differing Product Characteristics - Strength (15 mg, 45 mg vs. 10 mg, 20 mg, 40 mg, 60 mg, 80 mg with no overlap)
Indocin (indomethacin) - 25 mg, 50 mg oral capsules - 25 mg/5 mL oral suspension - 1 mg/vial powder for intravenous injection - 50 mg rectal suppositories - 1 to 2 capsules by mouth 2 to 3 times daily - 1 to 2 suppositories rectally 2 to 3 times daily	Orthographic Similarities - 'Iclusi' and 'Indoci' may appear similar when scripted - Both have 7 letters	Orthographic Differences - Down stroke in the 7 th position 'g' vs. no down stroke Differing Product Characteristics - Strength (15 mg, 45 mg vs. 25 mg, 50 mg, 25 mg/5 mL, 1 mg/vial with no overlap)

Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Infasurf (calfactant) - 30 mg/mL suspension - 3 mL/kg intratracheal at birth every 12 hours up to 3 doses	Orthographic Similarities - ‘Iclusi’ and ‘Infasu’ may appear similar when scripted	Orthographic Differences - Down stroke in the 7 th position ‘g’ vs. up and cross stroke in the 8 th position ‘f’ Differing Product Characteristics - Strength (15 mg, 45 mg vs. 30 mg/mL) - Dose (1 tablet vs. 3 mL/kg) - Setting of Use (Infasurf only used in NICU)
Intuniv (guanfacine) - 1 mg, 2 mg, 3 mg, 4 mg oral tablets - 1 tablet by mouth once daily	Orthographic Similarities - ‘Iclusi’ and ‘Intuni’ may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Dose (1 tablet) - Route of Administration (oral) - Frequency of Administration (once daily) - Dosage Form (tablets)	Orthographic Differences - Down stroke in the 7 th position ‘g’ vs. no down stroke Differing Product Characteristics - Strength (15 mg, 45 mg vs. 1 mg, 2 mg, 3 mg, 4 mg with no overlap)

Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Invanz (ertapenem) - 1 gm/vial powder for injection - 1 gm intravenous or intramuscular injection daily - 3 mo. to 12 years: 15 mg/kg intravenous or intramuscular injection twice daily	Orthographic Similarities - ‘Ic’ and ‘In’ may appear similar when scripted - ‘usig’ and ‘vanz’ may appear similar when scripted Phonetic Similarities - Both start with the letter ‘I’, which could be pronounced as ‘e’ Overlapping Product Characteristics - Frequency of Administration (once daily)	Orthographic Differences - 1 upstroke ‘l’ in the 3 rd position vs. no upstroke Phonetic Differences - ‘clusig’ and ‘nvanz’ sound different when spoken Differing Product Characteristics - Strength (15 mg, 45 mg vs. 1 gm with no overlap) - Dose (1 tablet vs. 1 gm or individualized dose based on weight)
Invega (paliperidone) - 1.5 mg, 3 mg, 6 mg, 9 mg - 1 tablet by mouth once daily	Orthographic Similarities - ‘Ic’ and ‘In’ may appear similar when scripted Overlapping Product Characteristics - Dose (1 tablet) - Route of Administration (oral) - Frequency of Administration (once daily) - Dosage Form (tablets)	Orthographic Differences - 1 upstroke ‘l’ in the 3 rd position vs. no upstroke - Position of the down stroke ‘g’: 7 th vs. 5 th positions Differing Product Characteristics - Strength (15 mg, 45 mg vs. 1.5 mg, 3 mg, 6 mg, 9 mg with no overlap)

Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Istodax (romidepsin) - 10 mg/vial powder with 2 mL diluent - 14 mg/m ² intravenous injection over 4 hours on days 1, 8, 15 of 28 day cycle	Orthographic Similarities - 'Iclu' and 'Isto' may appear similar when scripted - Both have 7 letters Phonetic Similarities - Both start with the same letter 'I'	Orthographic Differences - 'sig' and 'dax' appear different when scripted. No up stroke and 1 down stroke 'g' vs. 1 upstroke, 'd', and no down stroke. Phonetic Differences - clusig and stodax do not sound similar when spoken Differing Product Characteristics - Strength (15 mg, 45 mg vs. 10 mg with no overlap) - Dose (1 tablet vs. individualized dose based on BSA)
Letairis (ambrisentan) - 5 mg , 10 mg oral tablets - 1 tablet by mouth once daily	Orthographic Similarities - 'Iclu' and 'Leta' may appear similar when scripted Overlapping Product Characteristics - Dose (1 tablet) - Route of Administration (oral) - Frequency of Administration (once daily) - Dosage Form (tablets)	Orthographic Differences - Down stroke in the 7 th position 'g' vs. no down strokes Differing Product Characteristics - Strength (15 mg, 45 mg vs. 5 mg, 10 mg with no overlap)

Proposed Name: Iclusig (ponatinib) Strength and Dosage Form: 15 mg, 45 mg oral tablets Usual Dose: 45 mg once daily (15 mg or 30 mg once daily if adverse events)	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Zolinza (vorinostat) - 100 mg oral capsules - 3 to 4 capsules by mouth once daily	Orthographic Similarities - 'Iclus' and 'Zolin' may appear similar when scripted - Both have 7 letters Overlapping Product Characteristics - Route of Administration (oral) - Frequency of Administration (once daily)	Orthographic Differences - Down stroke in the 7 th position 'g' vs. down stroke in the 6 th position 'z' Differing Product Characteristics - Strength (15 mg, 45 mg vs. 100 mg with no overlap)

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/s/

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08/20/2012

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08/21/2012