CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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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--Final

Date	January 19, 2012
Reviewer(s)	Denise V. Baugh, PharmD, BCPS Division of Medication Error Prevention and Analysis
Team Leader	Lubna Merchant, PharmD, M.S. Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, R.Ph. Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s)	Inlyta (Axitinib) Tablets 1 mg, 5 mg
Application Type/Number:	NDA 202324
Applicant	Pfizer, Inc.
OSE RCM #	2011-3245

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

CONTENTS

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Inlyta is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, *Inlyta*, acceptable in OSE Review 2011-1314 dated July 7, 2011.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review # 2011-1314. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded no new names, thought to look or sound similar to Inlyta and represent a potential source of drug name confusion.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of January 9, 2012. The Office of Prescription Drug Promotion (OPDP) re-reviewed the proposed name on November 10, 2011 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Inlyta, did not identify any vulnerability that would result in medication errors with any additional name(s) noted in this review. Thus, DMEPA has no objection to the proprietary name, Inlyta, for this product at this time.

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

If you have further questions or need clarifications, please contact Mark Liberatore, OSE project manager, at 301-796-2221.

4 REFERENCES

1. OSE Reviews

OSE Review# 2009-150. *DMEPA Proprietary Name Review* for *Inlyta (Axitinib) Tablets 1mg and 5 mg;* Richard Abate, RPh, MS, May 22, 2009.

OSE Review# 2011-1314. *DMEPA Proprietary Name Review* for *Inlyta (Axitinib) Tablets 1mg and 5 mg;* Denise V. Baugh, PharmD, BCPS, July 7, 2011.

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/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?)

USAN Stems List contains all the recognized USAN stems.

4. Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

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

/s/

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01/19/2012

LUBNA A MERCHANT
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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:	July 7, 2011
Application Types/Numbers:	NDA 202324
Through:	Todd Bridges, RPh, Team Leader Kellie Taylor, PharmD, MPH, Associate Director Carol Holquist, RPh, Division Director Division of Medication Error Prevention and Analysis
From:	Denise V. Baugh, PharmD, BCPS, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name and Strengths:	Inlyta (Axitinib) Tablets 1 mg, 5 mg
Applicant:	Pfizer, Inc.
OSE RCM #:	2011-1314

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CONTENTS

EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, Inlyta for Axitinib Tablets. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Inlyta, acceptable for this product. DMEPA will notify the Applicant of these findings via letter.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request received from Pfizer, Inc., submitted April 13, 2011, to evaluate the proposed proprietary name, Inlyta, regarding promotional concerns and potential name confusion with other proprietary or established drug names based on the product characteristics provided by the Applicant.

The Applicant also submitted container labels and carton labeling which will be reviewed under separate cover (OSE Review #2011-1316).

1.2 REGULATORY HISTORY

Axitinib is the established name for the proposed proprietary name, Inlyta, previously found acceptable by DMEPA (OSE Review # 2009-150 dated May 22, 2009) under IND# 63,662. No product characteristic changes have been made since our last review of this name.

1.3 PRODUCT INFORMATION

Inlyta (axitinib) tablets is a tyrosine kinase inhibitor which will be indicated for the treatment of metastatic renal cell carcinoma after disease progression on prior systemic therapy. The product will be available in 1 mg and 5 mg tablets. The intended starting dose for Inlyta will be 5 mg (one tablet) taken orally twice a day. The dose may be adjusted upward based on patient tolerance or downward based upon adverse drug effects to Inlyta. The other possible doses of Inlyta include 2 mg (2 x 1 mg tablets), 3 mg (3 x 1 mg tablets), 7 mg (2 x 1 mg and 1 x 5 mg tablets) or 10 mg (2 x 5 mg tablets) taken twice daily. Inlyta will be available in bottles containing (b) (4) tablets which will be stored at room temperature (b) (4).

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 specific information associated with the methodology for the proposed proprietary name, Inlyta.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'I' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[1,2]

To identify drug names that may look similar to Inlyta, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (three, capital letter 'I', and lowercase 'l' and 't'), down strokes (one, lower case 'y'), cross strokes (one, lower case 't'), and dotted letters (none). Additionally, several letters in Inlyta 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 Inlyta.

When searching to identify potential names that may sound similar to Inlyta, the DMEPA staff search for names with similar number of syllables (three), stresses (IN-lie-tah, in-LIE-tah, or in-lie-TAH), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'Inly-' may sound like 'Inligh-' or 'Enlie'(See Appendix B). The Applicant's intended pronunciation (in-LIE-tah) was also taken into consideration, as it was included in the Proprietary Name Review Request. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

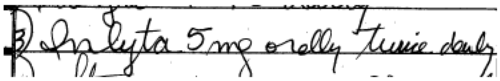
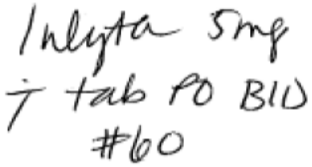
2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

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

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

Figure 1. Inlyta Prescription Study (conducted on May 12, 2011)

HANDWRITTEN PRESCRIPTION and MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Prescription: 	"Inlyta 5 mg tablets – take 1 tablet orally twice daily Dispense #60"
Outpatient Prescription: 	

3 RESULTS

The following sections describe DMEPA's findings from the database searches, CDER Expert Panel Discussion, and FDA prescription analysis studies.

3.1 DATA BASE AND INFORMATION SOURCES

The DMEPA safety evaluator searches yielded a total of 23 names as having some similarity to the proposed proprietary name Inlyta.

Eighteen of the 23 names (Trilyte, Levlite, Colyte, Embeda, Ionil-T, Indian Ink, Intal, Infalyte, Inspra, Isolyte, Lufyllin, Benlysta, Introl, Intron A, Enlon, Nalfon, Nulev, and Lubrin) were thought to look like Inlyta. Five names, (b) (4) Onglyza, Emcyt, Kinlytic, and Inlyta were thought to look and sound like Inlyta.

A search of the United States Adopted Name stem list on June 19, 2011, did not identify any United States Adopted Names (USAN) stem within the proposed name, Inlyta.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA safety evaluators (see Section 3.1 above) and did not identify additional names which were thought to have phonetic or orthographic similarity to Inlyta.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 27 practitioners responded and none of the names overlapped with existing names. Seventeen (n = 17) of the participants interpreted the name correctly as 'Inlyta' with correct interpretation occurring in the inpatient (n = 8) and outpatient (n = 9) studies. The remainder of the responses misinterpreted the drug name. Common misinterpretations included mistaking the first letter 'I' for the letter 'E and the letter 'y' for 'i' or 'ee' or 'ea'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF DRUG ONCOLOGY PRODUCTS (DDOP)

3.4.1 Initial Phase of Review

In response to the OSE April 28, 2011, e-mail, the Division of Drug Oncology Products stated that the Division is "fine with the name Inlyta, no issues".

3.4.2 Midpoint of Review

On June 30, 2011, DMEPA notified DDOP via e-mail that we find the name, Inlyta, acceptable. Per e-mail correspondence from DDOP on July 7, 2011, they "had no objections" to the proposed name, Inlyta.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Nine names (Trilyte, Colyte, Intal, Inspra, Isolyte, Emcyte, Kinlytic, Inlyta, and Enlon) were identified in our databases as well as in our previous review (OSE Review # 2009-150 dated May 22, 2009) and there were no changes in product characteristics. Therefore, these names were not evaluated further. Additionally, the primary safety evaluator identified one additional name, 'Isoptin', thought to look similar to Inlyta and represent a potential source of drug name confusion.

As such, a total of 15 names were further analyzed to determine if the drug names could be confused with Inlyta and if the drug name confusion would likely result in a medication error in the usual practice setting. Fourteen *new* names were identified in our database search and one name was identified in our independent search of names similar to Inlyta.

4 DISCUSSION

The proposed name, Inlyta, was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. Furthermore, we sought input from pertinent disciplines involved with the review of this application and considered it 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. The Division of Drug Oncology Products (DDOP), and DMEPA concurred with the promotional assessment.

4.2 SAFETY ASSESSMENT

DMEPA identified 15 names for their potential similarity to the proposed name, Inlyta. No other aspect of the name was identified as a potential source of confusion. Upon evaluation of the similar names, ten of the 15 names were eliminated from further consideration for the reasons stated in Appendices D through F.

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining five names and lead to medication errors. This analysis determined that the name similarity between Inlyta and the identified names was unlikely to result in medication errors with all of the products identified for the reasons presented in Appendix G.

5 CONCLUSIONS AND RECOMMENDATIONS

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

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 Sarah Simon, OSE Project Manager for the Division of Drug Oncology Products, at 301-796-5205.

6 PRIOR OSE REVIEW

OSE Review# 2009-150. *DMEPA Proprietary Name Review* for *Inlyta (Axitinib) Tablets 1mg and 5 mg;* Richard Abate, RPh, MS, May 22, 2009.

7 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)

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

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

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and 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)

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions

APPENDICES

Appendix A:

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. 3

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. 4 DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

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

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

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

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.[5] DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

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

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/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 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. 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.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not

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

convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

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

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

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

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

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

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

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in proposed name, Inlyta	Scripted may appear as	Spoken may be interpreted as
Capital 'I'	A, D, J, L, lower case l, P, S, or T	any vowel
Lower case 'I'	c, e, or l	any vowel
lower case 'n'	h, m, r, s, t, u, v, or x	'l' or 'm'
lower case 'l'	b, c, e, or i	'n'
lower case 'y'	'ij,' u, or z	any vowel
lower case 't'	f, r, or x	'd'
Lower case 'a'	c, 'ci,' 'ce.' o, u, or x	any vowel

Appendix C: FDA Prescription Study Responses for Inlyta (conducted May 12, 2011)

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Inlyta	Inlyta	Enleeta
Inlyta	Inlyta	Enlyta
Inlyta	Inlyta	Enleeta
Inlyta	Inlyta	Enlita
Inlyta	Inlyta	Enlida
Inlyta	Inlyta	Enleaga
Inlyta	Inlyta	Inlita
Inlyta	Inlyta	Inleadta
	Inlyta	Inlita
		Enlita

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

Proprietary Name	Similarity to Inlyta
Levlite	Look
Ionil-T	Look
Indian Ink	Look
Lufyllin	Look
Benlysta	Look
Nalfon	Look
Nulev	Look
Lubrin	Look

Appendix E: Drug name found in Clinical Pharmacology but not found in other drug databases (listed in References)

Proprietary Name	Comments
Introl (Glycerin) Oral Solution 75%	Clinical Pharmacology suggests product has been taken off the market

Appendix F. Drug name that has not been marketed in the US

Proprietary Name	Comments
(b) (4)	

*** **Note: This is proprietary and confidential information that should not be released to the public.*****

Appendix G: Potentially confusing names with orthographic and/or phonetic differences and differentiating product characteristics that decrease the risk of medication errors.

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale:**
Proposed name: **Inlyta (Axitinib) Tablet**	**Strength:** **1 mg and 5 mg**	**5 mg orally twice daily**
Infalyte (chloride, citrate, dextrose, potassium, sodium) oral electrolyte solution Usual dose: Goal is one to two ounces per pound of body weight over 2 to 4 hours beginning with teaspoonful every 10 to 15 minutes for 30 minutes, then gradually titrate up depending upon tolerance and response to product.	Orthographic similarity stems from sharing the same first two letters ('In-') and the same three letter combination ('-lyt-') within their names. An overlapping product characteristic includes route of administration (oral).	The marketed name, Infalyte, includes an additional up stroke ('f') in its infix as well as an additional letter 'a' prior to the shared letters, 'lyte'. This gives this name a different shape from the proposed name, Inlyta, and may help to differentiate this name pair. Differing product characteristics include dose (1 teaspoonful vs. 5 mg) and frequency of administration (every 10 to 15 minutes vs. twice daily). Inlyta is available in two strengths which must be provided by the prescriber prior to dispensing/administering this drug product.
Embeda (Morphine Sulfate and Naltrexone HCL) Capsule 20 mg/0.8 mg, 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, and 100 mg/4 mg Usual dose: Varies with level of patient pain and past exposure to opiates. Generally, begin with smallest strength and titrate up with a frequency of once daily to twice daily.	Orthographic similarity stems from the similar appearance of their first letters ('E' vs. 'I') in some handwriting samples, the presence of two up strokes ('b' and 'd' vs. 'l' and 't') in the same locations within their names, and the fact that both names end with the same letter ('a'). Phonetic similarity stems from both names having three syllables and the similar sounds made with letters within their names. For instance, it is difficult to distinguish the combination letters 'Em-' (in Embeda) from an 'In-' (in Inlyta) and 'da' and 'ta' (Embeda and Inlyta	The proposed proprietary name, Inlyta contains a down stroke ('y') and a cross stroke ('t') in its name which gives this name a different shape from the marketed name, Embeda. This distinction may help to differentiate these names from each other. Inlyta and Embeda are available in different strengths which must be specified by the prescriber to dispense/administer the medication as intended. Additionally, Embeda is a combination product. Therefore, despite the numerical overlap (e.g., 50 mg/2 mg vs. 5 mg) in strength, the prescriber would have to omit the second number (in this case 2 mg) on the prescription for Embeda and dispense/administer ten 5 mg tablets of Inlyta for a medication error to occur. This combination of events is unlikely.

	respectively) when spoken. Overlapping product characteristics include route of administration (oral) and frequency of administration (twice daily). Numerical overlap exists (100 mg/4 mg vs 1 mg, 50 mg/2 mg vs 5 mg).	

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale:**
Proposed name: **Inlyta (Axitinib) Tablet**	**Strength:** **1 mg and 5 mg**	**5 mg orally twice daily**
Intron A (Interferon alpha 2b) Injection 6 million units/mL, 10 million units/mL For injection: 10 million units/vial, 18 million units/vial, and 50 million units/vial Usual dose: 30 million units/m^2 subcutaneous or intramuscularly 3 times per week or 3 million units to 10 million units subcutaneously or intramuscularly 3 times per week depending upon diagnosis	Orthographic similarity stems from both names sharing the first two letters ('In-') followed by an up stroke ('t' vs. 'l'). Numerical overlap in strengths exists (10 million units/vial vs. 1 mg)	The marketed name, Intron, has only one up stroke ('t') whereas the proposed name, Inlyta, includes two up strokes ('l' and 't') with a down stroke ('y') between them. These features give these names different shapes and are likely to help distinguish between them when written. Differing product characteristics include dose and units of measurement (30 million units/m^2 or 3 million units to 10 million units vs. 5 mg), route of administration (subcutaneously or intramuscularly vs. oral), and frequency of administration (3 times weekly vs. twice daily). Inlyta and Intron A are available in different strengths which must be specified by the prescriber to dispense/administer the medication as intended.
Onglyza (Saxagliptin) Tablet 2.5 mg, 5 mg Usual dose: Take 2.5 mg or 5 mg orally daily	Orthographic similarity stems from the similar appearance of their first letters ('O' vs. 'I') when written and both names have an up stroke ('l'). Additionally, both names may have a cross stroke in similar positions within their names ('z' vs. 't') and both names end with the letter 'a'. Phonetic similarity stems from both names having three syllables and the same terminal letter, 'a'. Additionally, their infixes sound similar when spoken ('-lyz-' vs. '-lyt-').	The proposed name, Inlyta, includes two up strokes ('l' and 't') separated by a down stroke ('y') whereas the marketed name, Onglyza, has two down strokes ('g' and 'y') separated by a single up stroke ('l'). These features gives these names a different shape and may help to distinguish them from each other. One differing product characteristic is the frequency of administration (once daily vs. twice daily). Inlyta and Onglyza are available in different strengths which must be specified by the prescriber to dispense/administer the medication as intended.

	One overlapping product characteristic is the route of administration (oral). An overlapping strength exists, 5 mg.	

Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale:**
Proposed name: **Inlyta (Axitinib) Tablet**	**Strength:** **1 mg and 5 mg**	**5 mg orally twice daily**
Isoptin (Verapamil) Tablet 40 mg, 80 mg, 120 mg Isoptin brand discontinued but generics are available in the marketplace *Usual dose*: 80 mg to 120 mg three times daily	Orthographic similarity stems from the fact that this name pair shares the first letter ('I'), have a single down stroke ('p' vs. 'y'), and have a cross stroke ('t') within their names. Additionally, the appearance of the ending of these names ('-tin' vs. '-ta') may appear similar in some handwriting samples. Shared product characteristics include the dosage form (tablet) and route of administration (oral).	The proposed name, Inlyta includes an additional up stroke ('l') which precedes the sole down-stroke in this name. This difference gives these names different shapes and may help to distinguish these names from each other. Differing product characteristics include dose and (40 mg to 120 mg vs. 1 mg and 5 mg) and frequency of administration (three times daily vs. twice daily). Inlyta and Isoptin are available in different strengths which must be specified by the prescriber to dispense/administer the medication as intended.

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/s/

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