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

Date:	September 6, 2011
Reviewer:	Lissa C. Owens, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader:	Carlos Mena-Grillasca RPh, Team Leader Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
Drug Name & Strength(s):	Jakafi (Ruxolitinib Phosphate) Tablets 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg
Application Type/Number:	NDA 202192
Sponsor:	Incyte Corporation
OSE RCM #:	2011-2318

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Jakafi, 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 BACKGROUND

This review responds to a request from the Sponsor, Incyte Corporation, dated June 10, 2011 for a promotional and safety assessment of the proposed proprietary name, Jakafi. The Sponsor submitted an external study in support of their proposed proprietary name.

1.2 PRODUCT INFORMATION

Jakafi is an inhibitor of the Janus kinase family of protein tyrosine kinases (JAK's) that is used in the treatment of myelofibrosis. The recommended starting dose is dependent on platelet count starting at either 15 mg twice daily or 20 mg twice daily with dose adjustments in 5 mg twice daily increments. The maximum daily dose recommended is 50 mg (25 mg twice daily). In patients taking concomitant potent CYP3A4 inhibitors Jakafi is dosed once a day. In patients with hepatic impairment a 25% to 50% dose reduction is recommended. Jakafi will be available in 5 mg, 10 mg, 15 mg, 20 mg and 25 mg tablets. Jakafi will be supplied in 60-count bottles to be stored at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F).

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Jakafi.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'J' 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 Jakafi, 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 (two, capital letter 'J' and lower case 'k'), one down strokes (lower case 'f'), cross strokes (one, lower case 'f'), and dotted (one, lower case i). Additionally, several letters in Jakafi

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

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

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 Jakafi.

When searching to identify potential names that may sound similar to Jakafi, the DMEPA staff search for names with similar number of syllables (three), stresses (JA-ka-fi, ja-KA-fi or ja-ka-FI), and placement of vowel and consonant sounds (See Appendix B). The Sponsor's intended pronunciation (jak' ah fee) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, an inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies. (See Appendix C for samples and results).

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in the usual practice settings. After the Safety Evaluator has determined the overall risk associated with the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

The following sections describe the findings from our database searches, expert panel discussion, prescription analysis studies and safety evaluator risk assessment.

3.1 DATA BASE AND INFORMATION SOURCES

The DMEPA safety evaluator searches yielded a total of 12 names as having some similarity to the name Jakafi.

Eleven of the twelve names were thought to look like Jakafi. They are: Tikosyn, Jinteli, Tekral, Tekamlo, Tykerb, (b) (4) Noxafil, Jenloga, Javavi, Tokelu, and Totect. The remaining name was thought to look and sound similar to Jakafi: Jakafi.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of August 1, 2011.

3.2 EXPERT PANEL DISCUSSION

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

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

3.3 PRESCRIPTION ANALYSIS STUDIES

A total of 39 practitioners responded to the prescription analysis studies and none of the responses overlap with existing marketed products. Twenty-two participants interpreted the name correctly, all in the written prescription studies. All the participants in the verbal study misinterpreted the name. Most of the written responses in the verbal study misinterpreted the letter 'J' as the letters 'Ch' and the ending letter 'i' as the letters 'ee'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

The proprietary name risk assessment submitted by Incyte, found the proposed proprietary name acceptable. In the external name risk assessment submitted by the Sponsor, (b) (4) identified and evaluated a total of 2 drug names: Jalyn and Jantoven. These two names were added to the safety evaluator's assessment.

3.5 SAFETY EVALUATOR SEARCHES

Independent searches by the primary Safety Evaluator did not identify any additional names which were thought to look or sound similar to Jakafi and represent a potential source of drug name confusion. Thus, we identified a total of 14 names as having some similarity to the proposed proprietary name.

One of the 14 names "Jakafi" was eliminated since it was identified on the U.S. Patent and Trademark Office website registered to the Applicant for this product. Thus, a total of 13 names moved forward for evaluation: 2 identified in the External Study submitted by the Applicant and 11 identified in section 3.1 above.

3.6 Comments from the Division of Hematology (DHP)

3.6.1 Initial Phase of Review

In response to the OSE, June 29, 2011 e-mail, DHP forwarded concerns about the proposed name and the use of the pathway, 'JAK' in the name at the initial phase of the name review.

3.6.2 Midpoint of Review

DMEPA notified DHP via e-mail that we found the proposed name, Jakafi, acceptable on August 26, 2011. Per e-mail correspondence from DHP on September 2, 2011, they indicated that they had no objections to the proposed proprietary name, Jakafi.

4 DISCUSSION

This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered their comments accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns with the proposed name, Jakafi, from a promotional perspective. However, the division was concerned that the use of the "JAK" pathway in the proprietary name was misleading. DDMAC was made aware of the concern and they changed their opinion and objected to the name Jakafi on July 13, 2011. Before DMEPA issued the denial letter, the sponsor learned of DDMAC's concern with their proposed name and on July 22, 2011 submitted via email background information in support of their proposed name. This information was later officially submitted as an amendment to the initial request for name review.

On August 1, 2011, DMEPA, DDMAC, and DHP met to discuss DDMAC's evaluation of the Sponsor's background package in support of their proposed proprietary name Jakafi. At the meeting DDMAC communicated that they re-evaluated their objection and changed their position based on the applicant's submission. DDMAC stated, "DDMAC does not feel that it has an appropriate regulatory basis to uphold an objection to the proposed proprietary names from a promotional perspective based only on the fact that the proposed site of drug activity is embedded within the names. Therefore, upon further consideration, DDMAC does not have any objections to the proposed proprietary names, (b) (4) and Jakafi, from a promotional perspective".

DMEPA and DHP concurred with DDMAC's final promotional evaluation of the proposed proprietary name Jakafi.

4.2 SAFETY ASSESSMENT

DMEPA identified 13 names for their potential similarity in sound and spelling to the proposed name, Jakafi. We did not identify any other aspects of the name that would be considered as a potential source for error.

Three of the thirteen potentially similar names did not undergo failure mode and effect analysis (FMEA) for the following reasons: No additional information in our internal databases and common drug references, proposed proprietary name that was denied, and the name of a medical condition (see Appendix D).

Failure mode and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the remaining 10 names and lead to medication errors. This analysis determined that the name similarity between Jakafi and

all of the identified names was unlikely to result in medication error for the reasons presented in Appendix E.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Jakafi, 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, Jakafi, 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 Sue Kang, OSE Project Manager, at 301-796-4216.

5.1 COMMENTS TO THE APPLICANT

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

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

If any of the proposed product characteristics as stated in your June 10, 2011 submission are altered the name must be resubmitted for review. The conclusions upon re-review are subject to change.

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks

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/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and

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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.

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 letters	• 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.

		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. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[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.

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

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 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), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

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

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

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Jakafi	Scripted may appear as	Spoken may be interpreted as
Capital 'J'	'T', 'Z', 'I', and 'Y'	'G', Ch
lower case 'a'	'c', 'ce,' 'ci,' 'd', 'e', 'o' or 'u'	Any vowel
lower case 'k'	"n','x', 'h', 'la'	'c' or 'g'
lower case 'f'	't'	'v'
lower case 'i'	Any vowel	'ee'. 'y' and any vowel

Appendix C: FDA Prescription Study for Jakafi

Figure 1. Jakafi Study Samples (conducted on June 24, 2011)

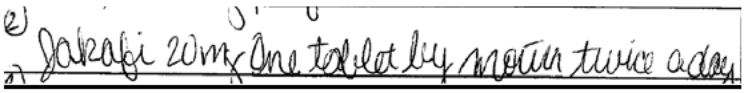
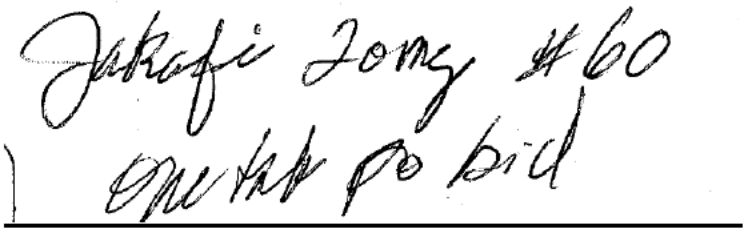
HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Medication Order 	Jakafi 20 mg One tablet by mouth twice a day #30
Outpatient Rx 	

Table 1: Responses to Prescription Study

Outpatient Prescription	Inpatient Medication Order	Voice Prescription
Jakarfi	Jakafi	Chicoffe
Jarafi	Jakafi	Chacoffee
Jakafi	Jakafi	Chicoffee
Jakafi	Jakafi	Chicoffe
Jakafi	Jakafi	Chicofee
Jarofic	Jakafi	Jicoffy
Jakafi	Jakafi	Chickoffee
Jakafic	Jakafi	Chicoffee
Jakafic	Jakafi	Chicaphi
Jakafi	Jakafi	Jacafe
Jakafi	Jakafi	Chicoffee
Jakafi	Jakafi	Jecoffee
	Jakafi	
	Jakafi	
	Jakafi	

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

Proprietary Name	Active Ingredient	Noted Similarity to Jakafi	Failure preventions
Javavi	Not Listed	Look	Found on POCA as a proprietary name entered to the database by a Safety Evaluator. However, the name is not in the Proposed Names List. Therefore it seems to be a typo. No additional information was available elsewhere (i.e. L: drive, AIMS, or in common drug references).
Tokelu	None	Look	Found on Micromedex. It is another name for the medical condition 'Tinea imbricata'.
(b) (4)			

Appendix E: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Jakafi (Ruxolitinib Phosphate)		5 mg, 10 mg, 15 mg, 20 mg, and 25 mg Tablets	15 to 25 mg twice a day	
Tekamlo (Aliskeren hemifumarate and Amlodipine besylate) ***Orthographic similarities**: The letters 'J' and 'T' when scripted can look similar. Both names have an upstroke letter, 'k' in the third position.*	Look	150 mg/5 mg, 150 mg/10 mg, 300 mg/5 mg, 300 mg/ 10 mg Tablets	One tablet once a day	**Orthographic differences:** The ending letters of Jakafi, 'afi' and the ending letters of Tekamlo, 'mlo' help to differentiate between the two names.
Tikosyn (Miglustat) ***Orthographic similarities**: The letters 'J' and 'T' when scripted can look similar. Both names have an upstroke letter, 'k' in the third position.*	Look	0.125 mg, 0.25 mg, 0.5 mg Capsules	0.125 mg to 0.5 mg twice a day	**Orthographic differences:** When scripted the ending of Jakafi 'afi' looks different than Tikosyn, 'syn'.
Jalyn (Dutasteride and Tamsulosin hydrochloride) ***Orthographic similarities**: They both begin with the same letter string 'Ja' followed by an upstroke 'k' in Jakafi and 'l' in Jalyn.*	Look	0.5 mg/0.4 mg Capsule	One capsule once a day	**Strength:** Multiple strengths vs. Single strength **Orthographic differences:** The ending letters of Jakafi, 'afi' and the ending letters of Jalyn, 'lyn' help to differentiate between the two names.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Jakafi (Ruxolitinib Phosphate)		5 mg, 10 mg, 15 mg, 20 mg, and 25 mg Tablets	15 to 25 mg twice a day	
Jinteli (Norethindrone and Ethinyl estradiol) ***Orthographic similarities**: Both begin with similar letter strings 'Ja' and 'Ji' which when scripted may look similar. Both share the common letters, 'J,' and 'i'*	Look	1 mg/0.05 mg Tablets	One tablet once a day	**Strength:** Multiple strengths vs. Single strength **Orthographic differences:** Jakafi has an upstroke letter 'k' in the third position vs. Jinteli which does not. Jakafi has one dotted letter 'i' vs. Jinteli which has two dotter letter 'i'.
Tekral Diphenhydramine and Pseudoephedrine hcl) ***Orthographic similarities:** The letters 'J' and 'T' when scripted can look similar. Both names have an upstroke letter, 'k' in the third position*	Look	100 mg/120 mg Tablets	One tablet every 12 hours	**Strength:** Multiple strengths vs. Single strength **Orthographic differences:** The ending letters of Jakafi, 'afi' and the ending letters of Tekral, 'ral' help to differentiate between the two names. Jakafi has a downstroke letter 'f' in the 5th position vs. Tekral which does not have any downstroke letters. Jakafi has a dotted letter 'i' vs. Tekral which has no dotted letters.
Tykerb (Lapatinib) ***Orthographic similarities**: The letters 'J' and 'T' when scripted can look similar. Both names have an upstroke letter, 'k' in the third position*	Look	250 mg Tablets	Five to Six tablets once a day	**Strength:** Multiple strengths vs. Single strength **Dose:** One tablet vs. Multiple tablets **Orthographic differences** The ending letters of Jakafi, 'afi' and the ending letters of Tykerb, 'erb' help to differentiate between the two names. Jakafi has a downstroke letter 'f' in the 5th position vs. Tykerb which has a downstroke letter 'y' in the 2nd postion. Jakafi has a dotted letter 'i' vs. Tykerb which has no dotted letters.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Jakafi (Ruxolitinib Phosphate)		5 mg, 10 mg, 15 mg, 20 mg, and 25 mg Tablets	15 to 25 mg twice a day	
Noxafil (Posaconazole) ***Orthographic similarities**: Both share the common letters, 'a', 'f', and 'i'*	Look	40 mg/ml Suspension	100 mg to 400 mg two to three times a day	**Dosage Form:** Tablet vs. Suspension **Dosage:** Tablet vs. XX ml **Orthographic differences:** Jakafi has an upstroke letter 'k' in the 3rd position vs. Noxafil which does not.
Jenloga (Clonidine Hydrochloride) ***Orthographic similarities:** They both begin with similar letter strings 'Ja' and 'Je' that when scripted look similar*	Look	0.1 mg Tablets	0.1 mg to 0.6 mg in twice a day	**Strength:** Multiple strengths vs Single strength **Orthographic differences:** The ending letters of Jakafi, 'kafi' and the ending letters of Jenloga, 'loga' help to differentiate between the two names. Jakafi has one dotted letter 'i' vs. Jenloga which has no dotted letters.
Jantoven (Warfarin) ***Orthographic similarities:** They both begin with the same letter string 'Ja'. Both share the common letters, 'J' and 'a''*	Look	1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, 10 mg Tablets	Varies per patient	**Orthographic differences:** Jakafi has 6 letters and may appear shorter when scripted vs. Jantoven which has 8 letters The ending letters of Jakafi, 'kafi' and the ending letters of Jantoven, 'oven' help to differentiate between the two names. Jakafi has a dotted letter 'i' vs. Jantoven which has no dotted letters.
Totect (Dexrazoxane) ***Orthographic similarities**: The letters 'J' and 'T' when scripted can look similar.*	Look	500 mg powder for Injection	Day one: 1000 mg/m2 Day two: 1000 mg/m2 Day three: 500 mg/m2	**Route of Administration:** Oral vs. Intravenous **Orthographic differences:** The ending letters of Jakafi, 'afi' and the ending letters of Totect, 'ect' help to differentiate between the two names. Jakafi has one dotted letter 'i' vs. Totect which has no dotted letters. Jakafi has a downstroke letter 'f' in the 5th position vs. Totect which has no dowstroke letters. Jakafi contains no cross stroke letters vs. Totect which has two cross stroke letter 't'

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/s/

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