CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-198

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	September 4, 2008
To:	Donna Griebel, MD Director, Division of Gastroenterology Products, HFD-180
Thru:	Kellie Taylor, Pharm D, MPH, Team Leader Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis, HFD-420
From:	Richard Abate, RPh, MS, Safety Evaluator Division of Medication Error Prevention and Analysis, HFD-420
Subject:	Proprietary Name Review (final) for Sancuso
Drug Name(s):	Sancuso (granisetron transdermal system) 3.1 mg/24 hours
Application Type/Number:	NDA 22-198
Applicant:	Strakan International Limited
OSE RCM #:	2007-1573

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

CONTENTS

EXECUTIVE SUMMARY 3
1 BACKGROUND 3
1.1 Introduction 3
1.2 Product Information 3
2 METHODS AND MATERIALS 3
2.1 Search Criteria 4
2.2 Safety Evaluator Risk Assessment of the Proposed Proprietary Name 6
3 RESULTS 9
3.1 Database and Information Sources 9
3.2 CDER Expert Panel Discussion 9
3.3 Safety Evaluator Risk Assessment 9
4 DISCUSSION 10
4.1 Concomitant Use of Oral and Transdermal Granisetron Products 10
5 CONCLUSIONS AND RECOMMENDATIONS 11
5.1 Comments to the Division 11
5.2 Comments to the Applicant 11
6 REFERENCES 12
6.1 Reviews 12
6.2 Databases 12
APPENDICES 14

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Sancuso, has some similarity to other proprietary drug names, but the findings of the FMEA indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. As such, the medication error prevention staff does not object to the use of the proprietary name, Sancuso, for this product. However, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

Our analysis identified a potential medication error related to patients receiving duplicate granisetron therapy and provides recommendations is Section 5.2 to help minimize the potential for this error at the product launch.

1 BACKGROUND

1.1 INTRODUCTION

This review in is response to a request from the Division of Gastroenterology for a final review of the proposed proprietary name, Sancuso. The Division of Medication Error Prevention and Analysis previously reviewed the name, Sancuso, without objection in OSE review # 2007-1573, Proprietary Name Review for Sancuso dated March 17, 2008. However, the review identified a risk of duplicate therapy resulting from concomitant use of oral and transdermal granisetron products.

This final review is necessary as it has been greater than 90 days since the prior review. In addition, the expression of product strength changed from 3.6 mg/24 hours to 3.1 mg/24 hours, thus requiring resubmission of the proposed proprietary name for review.

1.2 PRODUCT INFORMATION

Sancuso (granisetron) transdermal system is indicated for the prevention of nausea and vomiting in patients receiving moderately or highly emetogenic chemotherapy for up to five consecutive days. The patch is a new dosage form for granisetron. The patch, applied 24 to 48 hours prior to chemotherapy, delivers 3.1 mg of granisetron per 24 hour period and may be worn for up to seven days. The patch should not be removed for at least 24 hours after chemotherapy cycle is completed. The product will be packaged in cartons containing a single patch and stored at room temperature.

2 METHODS AND MATERIALS

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

For the proprietary name, Sancuso, the medication error prevention staff searches a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.2). Our Division also conducts internal CDER prescription analysis studies, and, when provided, external prescription analysis

studies results are considered and incorporated into the overall risk assessment. However, we did not include new prescription studies in this analysis as these were included in the previous name evaluation, OSE review 2007-1573, dated March 17, 2008.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.2). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [1] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The medication error prevention staff 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. [2] The medication error prevention staff uses their clinical expertise to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, the medication error prevention 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.[3]

2.1 SEARCH CRITERIA

The medication error prevention staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

---

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

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

[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

For this review, particular consideration was given to drug names beginning with the letter 'S' 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.[45]

To identify drug names that may look similar to Sancuso, the staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (one, capital letter 'S'), downstokes (none), cross-strokes (none), and dotted letters (none). Additionally, several letters in Sancuso may be vulnerable to ambiguity when scripted, including the letter 'S' may appear as 'G'; lower case 's' appear as a lower case 'g;' 'san-' may appear as 'cam-;' lower case 'a' may appear as lower case 'o' or 'u;' lower case 'n' may appear as lower case 'h,' 'm,' 'r;' 's,' 'u,' or 'x;' 'cu' may appear as 'ai;' lower case 'u' may appear as a lower case 'a' or 'o;' and lower case 'o' may appear as a lower case 'a' or 'u.' As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Sancuso.

When searching to identify potential names that may sound similar to Sancuso, the medication error prevention staff searches for names with similar number of syllables (three), stresses (san-CU-so or SAN-cu-so), and placement of vowel and consonant sounds. Additionally, several letters may be vulnerable to misinterpretation when spoken, including 's' misinterpreted as 'x' or 'z;' 'n' misinterpreted as 'm;' the short 'u' may be misinterpreted as 'oo;'and 'c,' may be misinterpreted as 'ck' or 'k.' As such, the staff also considers these alternate interpretations when identifying drug names that may sound similar to Sancuso. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the medication error prevention staff were provided with the following information about the proposed product: the proposed proprietary name (Sancuso), the established name (granisetron), proposed indication (the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to 5 consecutive days.), strength (3.1 mg/24 hours), dose (one patch), frequency of administration (once at least 24 hours prior to the start of chemotherapy), route (topical) and dosage form of the product (patch or transdermal system). Appendix A provides a more detailed listing of the product characteristics the Staff general takes into consideration.

Lastly, the medication error prevention staff also considers the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and we provide additional

---

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

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

comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1 Database and Information Sources

The proposed proprietary name, Sancuso, was provided to the medication error prevention staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Sancuso using the criteria outlined in 2.1. A standard description of the databases used in the searches is provided in Section 6.2. To complement the process, we 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 medication error prevention staff reviews the United States Adopted Name (USAN) stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the medication error prevention staff to gather CDER professional opinions on the safety of the product and the proprietary name, Sancuso. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the medication error prevention staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

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

2.2 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, the medication error prevention staff seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective then remedies available in the post-approval phase.

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

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

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Sancuso 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 Sancuso 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 and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The medication error prevention staff will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The medication error prevention staff identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, <u>and</u> demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. The medication error prevention staff identifies a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that the medication error prevention staff objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, we will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while we will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then the medication error prevention staff will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, the World Health Organization, the Joint Commission, and the Institute for Safe Medication Practices, that have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the medication error prevention staff contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

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

If the medication error prevention staff objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. We are likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for the medication error prevention staff to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name,

and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The medication error prevention staff conducted a search of the internet, several standard published databases and information sources (see Section 6 References) for existing drug names which sound-alike or look-alike to Sancuso to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, the staff identified 16 names as having some similarity to the name Sancuso.

Fifteen of the 16 names that were thought to look like Sancuso, which include: Sancago, ——— , San Cura, Sancazid, Sanctura, ——— Sanctura XR, Sancyan, Sangcya, Sansac, Sansert, Senecio, Senexon, Zanosar, and Zensana***. One additional name (Sancuso) was thought to look and sound similar to Sancuso. b(4)

A search of the United States Adopted Name stem list on August 28, 2008, identified no USAN stems within the proposed name, Sancuso.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by the medication error prevention staff (see section 3.1 above), and noted no additional names thought to have orthographic similarity to Sancuso.

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 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified no additional names thought to look or sound similar to Sancuso. As such, a total of 16 names were analyzed to determine if the drug names could be confused with Sancuso and if the drug name confusion would likely result in a medication error.

All of the 16 names were determined to have some orthographic and/or phonetic similarity to Sancuso, and thus determined to present some risk of confusion. Failure mode and effect analysis was then applied to determine if the potential name, Sancuso, could potentially be confused with any of the 16 names and lead to medication errors.

Three of the names were not evaluated further because confusion with these names was determined to be unlikely. Sancuso was identified as an internationally trademarked name by the Applicant but the product does not appear to be marketed in other countries yet. The name, Senecio, is a plant genus identified in Natural Medicines Comprehensive Database (See Section 6), but was not identified as an active ingredient or in the name of any product. The name, Sancyan, was identified as a chemical used in agriculture.

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

The Failure Mode and Effects Analysis determined that the name similarity between Sancuso and the remaining 13 identified names was unlikely to result in medication errors for all 13 products for reasons described/outlined in Appendices B through G.

Additionally, because the strength of the product had 3.1 mg per 24 hours the names identified in OSE Review 2008-1573 (dated March 17, 2008) were reassessed and it was determined that the change in strength did not affect the original risk assessment findings. b(4)

4 DISCUSSION

The Division of Medication Error Prevention and Analysis assessed 16 names for their potential for confusion with Sancuso. However, our FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. However, our risk assessment faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, the medication error prevention staff recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

4.1 CONCOMITANT USE OF ORAL AND TRANSDERMAL GRANISETRON PRODUCTS

As the Applicant for Sancuso differs from the Sponsor of Kytril, we note that some granisetron dosage forms will have different proprietary names. Because of this fact, we noted a potential medication error with the introduction of Sancuso to the market place in our prior review of the proprietary name.[7] The introduction of the granisetron patch formulation could lead to inadvertent use of the oral and transdermal formulations concurrently. Our Division's post-marketing surveillance of medication errors reveals that overdoses of medication occur when a prescriber, unfamiliar with all proprietary names of a medication, prescribes a medication to the patient who is already receiving the same medication under a different proprietary name. In addition, research in the hospital setting has shown prescribing the same or similar medication to be given concurrently by two routes of administration to be a common source of medication error.[8] The same study indicated the prescribing of the same or similar medication to be given concurrently via the transdermal and oral route of administration as the second most common type of prescribing error (the most common type was concurrent prescribing of same/similar medication by IV and oral routes). In these situations, the patient may receive an overdose, thus potentially leading to an adverse event. In addition, patients who previously received oral granisetron may be likely to be switched to the Sancuso patch to treat their chemotherapy

[7] OSE review 2007-1573, Proprietary Name Review for Sancuso, Abate, R. March 17, 2008.

[8] Lesar TS. Medication Prescribing Errors Involving Route of Administration. Hosp Pharmacy. 2006; 41(11): 1053-1066.

induced nausea and vomiting. These patients may continue to use any supply granisetron tablets available in the home increasing the potential for an overdose of granisetron. Finally, Sancuso provides granisetron in a new dosage form, a patch with which healthcare providers or patients may not be familiar, increasing the potential for a patient to receive additional oral or intravenous doses of granisetron while wearing this patch. Although several possibilities for error exist, it should be noted that the clinical reviewer of the application has considered the potential exposure, and it is our understanding that it is unlikely to present a safety risk.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Sancuso, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, DMEPA does not object to the use of the proprietary name, Sancuso, for this product. However, if **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, the medication error prevention staff rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

Additionally, we provide recommendations to the Applicant in Section 5.2 to help minimize the potential of duplicate granisetron therapy at the launch of Sancuso to the market place.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Applicant to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

5.1 COMMENTS TO THE DIVISION

The Division of Medication Error Prevention and Analysis would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Cherye Milburn, project manager, at 301-796-2084.

5.2 COMMENTS TO THE APPLICANT

The results of the Proprietary Name Risk Assessment found that the proposed name, Sancuso, has some similarity to other proprietary drug names, but the findings of the FMEA indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Sancuso, for this product. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the

product, the medication error prevention staff rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review.

5.2.1 New Dosage Form for Granisetron

As this is a new dosage form for granisetron, we anticipate the possibility of medications errors resulting in duplicate granisetron therapy (i.e. patients receiving oral or intravenous granisetron while wearing a Sancuso patch) especially at product launch. Therefore, at the time of product launch, the Division of Medication Error Prevention and Analysis recommends that the Applicant informs healthcare practitioners to avoid administering other granisetron containing products are administered to patients wearing a Sancuso patch.

6 REFERENCES

6.1 REVIEWS

1. ***OSE review 2007-1573, Proprietary Name Review for Sancuso, Abate, R. March 17, 2008.***

6.2 DATABASES

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

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

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

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

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

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

4. ***AMF Decision Support System [DSS]***

DSS is a government database used to track individual submissions and assignments in review divisions.

5. ***Division of Medication Error Prevention proprietary name consultation requests***

This is a list of proposed and pending names that is generated by the medication error prevention staff from the Access database/tracking system.

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

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

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

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

8. US Patent and Trademark Office http://www.uspto.gov.

Provides information regarding patent and trademarks.

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

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

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

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

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

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

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

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

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

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

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

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

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

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

Appendix B: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Sancuso	Country
Sancago	Look	Thailand
Sancazid	Look	Greece

Appendix C: Products discontinued from the market with no generic equivalent or was a branded generic product.

Proprietary Name	Similarity to Sancuso	Year product discontinued
San-Cura	Look	Unknown (trademark abandoned 1998)
Sangcya	Look	2000
Sansac	Look	Undetermined (branded generic)
Sansert	Look	2001

Appendix D: Products approved by the Agency with a different proprietary name or the application was withdrawn prior to action.

Proprietary Name	Similarity to Sancuso
[redacted]	Look
Zensana ***	Look

b(4)

Appendix E: Products with no numerical overlap in strength or dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Sancuso (Granisetron Transdermal System)		**Strengths: 3.1 mg/24 hours**	**Usual dose: Apply one patch at a minimum of 24 hours prior to the start of chemotherapy. The patch may be worn for up to 7 days.**
Sanctura, Sanctura XR	Look	20 mg , 60 mg	One tablet (20 mg) by mouth twice daily or One capsule (60 mg by mouth daily

Appendix F: Products with a single strength (Strength may be omitted when writing a prescription)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Other differentiating product characteristics (excluding dose and frequency)
Sancuso (Granisetron Transdermal System)		**Strengths: 3.1 mg/24 hours**	**Usual dose: Apply one patch at a minimum of 24 hours prior to the start of chemotherapy. The patch may be worn for up to 7 days.**	
Senexon	Look	8.6 mg	One to two tablets by mouth twice daily.	Senexon is an over-the-counter, dosage form, route of administration, indication for use.

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

Zanosar	Look	1 gram	500 mg/m^2 intravenously daily for five days or 1000 mg/m^2 intravenously weekly	Dosage form, route of administration, indication for use, Zanosar will be administered by a healthcare provider.

Appendix G: Potential confusing name with numerical overlap in strength

Sancuso (Granisetron Transdermal System)	**Strengths: 3.1 mg/24 hours**	**Usual dose: Apply one patch at a minimum of 24 hours prior to the start of chemotherapy. The patch may be worn for up to 7 days.**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**

b(4)

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

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

/s/

Richard Abate
9/4/2008 10:58:13 AM
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor
9/5/2008 12:37:43 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
9/5/2008 12:39:25 PM
DRUG SAFETY OFFICE REVIEWER

Division of Medication Error Prevention
Office of Surveillance and Epidemiology
HFD-420; White Oak 22, Room 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: October 1, 2007

NDA#: 22-198

NAME OF DRUG: Sancuso (Granisetron Transdermal System) 3.6 mg/24 hours

NDA HOLDER: Strakan International Limited

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

I. INTRODUCTION:

This consult was written in response to a request from the Division of Gastroenterology (HFD-180), for assessment of the proprietary name, "Sancuso," regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling provided for review and comment will be discussed in a separate review.

PRODUCT INFORMATION

Sancuso (granisetron) is indicated for the prevention of nausea and vomiting in patients receiving moderately or highly emetogenic chemotherapy for up to five consecutive days. The patch is a new dosage form for granisetron. The patch, applied 24 to 48 hours prior to chemotherapy, delivers ___ of granisetron per 24 hour period and may be worn for up to seven days. The patch should not be removed for at least 24 hours after chemotherapy cycle is completed. b(4)

II. RISK ASSESSMENT:

The Medication Error Staff conducted a search of the internet, several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Sancuso to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The Saegis[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel

[1] MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, and the electronic online version of the FDA Orange Book.
[4] Phonetic and Orthographic Computer Analysis (POCA)
[5] WWW location http://www.uspto.gov/tmdb/index.html.
[6] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

discussion was conducted to review all findings from the searches. In addition, our Division conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name. Following completion of these initial components, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a product must be considered in the overall safety evaluator risk assessment.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by the Medication Error Staff to gather professional opinions on the safety of the proprietary name Sancuso. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of Medication Error Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name, Sancuso, acceptable from a promotional perspective.

2. The Expert Panel identified six proprietary names that were thought to have the potential for confusion with Sancuso. In addition, the Expert Panel raised a concern about potential medication error issues regarding this product. Specifically, the product name, Sancuso, creates dual trade name for the established name, granisetron.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Sancuso 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. These studies employed a total of 123 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Sancuso. (See page 4.) These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were 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 sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Sancuso #3 Apply 1 patch every 7 days	Sancuso #3 Apply 1 patch every 7 days
Inpatient RX: Sancuso apply 1 patch q 7 days	

2. Results:

   None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Sancuso, the Expert Panel identified six names that were thought to have the potential to be confused with Sancuso. These names include Gantrisin, Lantus, Panscol, Sanctura, Sangcya, and Sansac. In addition, the panel also raised concerns regarding expression of strength, dual tradenames and problems associated with patches. Independent analysis identified five additional names, Gaviscon, ——— Sambucol, Sancase (South Korea), and Sancugo (Malaysia), that were that to have the potential to be confused with the proprietary name, Sancuso. **b(4)**

Additionally, the Medication Error Staff conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Sancuso. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size.

Upon further review of the aforementioned names, nine names, Gantrisin, Gaviscon, ——— Lantus, Pansol, Sambucol, Sanctura, Sangcya, and Sansac, were not considered further due to lack of significant look-alike and/or sound-alike similarities with Sancuso. In addition, these products have multiple differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, dosage formulation, therapeutic class, storage conditions, patient population, prescriber population, product availability, and/or type of marketing or distribution. In addition, the remaining two names, Sancase (South Korea) and Sancugo (Malaysia), were not reviewed further as they are marketing outside the U.S. Therefore, no names require further discussion in this review from a sound and look-alike perspective. **b(4)**

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

However, the Medication Error Staff does have medication error safety concerns with the proposed name, Sancuso, which are discussed in further detail below.

1. Concomitant use of oral and transdermal granisetron products.

   Granisetron is currently marketed under the proprietary name Kytril® as an oral tablet, an oral solution, and injection dosages forms. Generic equivalent products exist for the oral tablet and injection dosage forms, but none of these generic products have a proprietary name. We note the Applicant for Sancuso differs from the maker of Kytril®.

   The Expert Panel raised concerns about the occurrence of duplicate therapy medication errors. The introduction of the granisetron patch formulation could lead to inadvertent use of the oral and transdermal formulations concurrently. Our Division's postmarketing surveillance of medication errors reveals that overdoses of medication occur when a prescriber, unfamiliar with all proprietary names of a medication, prescribes a medication to the patient who is already receiving the same medication under a different proprietary name. In addition, research in the hospital setting has shown the prescribing the same or similar medication to be given concurrently by two routes of administration to be a common source of medication error.[7] The same study indicated the prescribing of the same or similar medication to be given concurrently via the transdermal and oral route of administration as the second most common type of prescribing error (the most common type was concurrent prescribing of same/similar medication by IV and oral routes). In these situations, the patient may receive an overdose, thus potentially leading to an adverse event. In addition, patients who previously received oral granistetron may be likely to be switched to the Sancuso patch to treat their chemotherapy induced nausea and vomiting. These patients may continue to use any supply granisetron tablets available in the home increasing the potential for an overdose of granisetron. Finally, Sancuso provides granisetron in a new dosage form, a patch with which healthcare providers or patients may not be familiar, increasing the potential for a patient to receive additional oral or intravenous doses of granisetron while wearing this patch.

   The Medication Error Staff believes that the potential for overdose exists with concomitant use of granisetron products via different routes of administration (i.e. transdermal and oral). However in this case, the elevated levels of granisetron may not result in an adverse event as higher doses of granisetron have been studied without apparent adverse effects. We also note that granisetron has a large therapeutic window in that a single intravenous dose as high as 38.5 mg has been given to patients without adverse consequences. The pharmacokinetic parameters of granisetron from Sancuso in healthy subjects note the Cmax averages 5.0 ng/mL. The Cmax after a single 40 mcg/kg intravenous dose of Kytril®, four times the labeled dose for prevention of chemotherapy induced nausea and vomiting, results in an average drug plasma levels of 63.8 ng/mL.[8] If the patient is wearing a Sancuso patch and receives additional doses of granisetron, either orally or intravenously, as part of their chemotherapy administration, the facts that granisetron is well tolerated may reduce the potential harm caused by such an overdose. In addition, a search of the FDA's Adverse Event Reporting System database resulted in no reports involving overdoses of granisetron. Finally, both Sancuso and the potential additional doses of granisetron are likely to be the ordered by the same prescriber thus reducing the potential for prescribers to inadvertently order both products simultaneously. Nevertheless, the Division of Medication Error Prevention continues to be concerned that errors related to duplicate therapy

[7] Lesar TS. Medication Prescribing Errors Involving Route of Adminstration. Hosp Pharmacy. 2006; 41(11): 1053-1066.
[8] Kytril® package insert, Roche Laboratories, 2005

may occur with the introduction of a granisetron transdermal product with a new proprietary name.

The Medication Error Staff believes that the risk of concurrent therapy maybe reduced by using the same proprietary name for different dosage forms of a medication to assist healthcare practitioners and patients more readily identify the medication, even when given by different routes. However, we note the Applicant does not have rights to the existing proprietary name, Kytril®. Therefore, we believe the Applicant should implement an educational campaign at the market launch of Sancuso in an attempt to make healthcare practitioners, patients, and caregivers aware of the risk of concomitant therapy if used with Kytril® or other oral granisetron products.

III. CONCLUSION

The Safety Evaluator Risk Assessment findings indicate that the proposed name, Sancuso, does not appear vulnerable to name confusion that could lead to medication errors. We note it is likely that medication errors related to duplicate therapy will occur with the introduction of a granisetron containing transdermal patch regardless of the new proprietary name. Therefore, we do not object to the use of the proprietary name, Sancuso. for this product.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Medication Error Staff rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

IV COMMENTS TO THE APPLICANT

The Division of Medication Error Prevention does not object to the use of the proprietary name, Sancuso, for this product. However, we raised concerns about the occurrence of duplicate therapy medication errors as the introduction of the granisetron patch formulation could lead to inadvertent use of the oral and transdermal formulations concurrently. Therefore, we believe the Applicant should implement an educational campaign at the launch of marketing Sancuso in an attempt to make healthcare practitioners, patients, and caregivers aware of the risk of concomitant therapy if used with Kytril® or other oral granisetron products.

The Division of Medication Error Prevention would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. Please copy the Medication Error Staff on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Cherye Milburn, project manager, at 301-796-2084.

Appendix A Rx Study Responses

Outpatient	Inpatient	Verbal
Sancuso	Sancuso	Sancuso
Sancuso	Sancuso	Sancuso
Sancuso	Sancuso	Sancuso
Sanuiso	Sancuso	Sancuso
Sancuso	Sancuso	
Sancuso	Sancuso	
Sancuso	Sancuso	
Sancuso	Sancuso	
Sancuso	Sancusso	
Sanurso		
Sancuso		
Sancuso		
Sancuso		
Sancuso		
Sancuso		
Sancuso		
Sancuso		

APPEARS THIS WAY ON ORIGINAL

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

/s/

Richard Abate
3/17/2008 04:39:35 PM
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor
3/17/2008 04:41:02 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
3/17/2008 05:50:44 PM
DRUG SAFETY OFFICE REVIEWER