

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-275**

**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: April 7, 2009

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Subject: Proprietary Name Review

Drug Name: Samsca (Tolvaptan) Tablets  
15 mg and 30 mg

Application Type/Number: NDA 22-275

Applicant: Otsuka Pharmaceuticals

OSE RCM #: 2008-1856

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

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## EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that, Samsca, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Samsca, for this product.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and recommends that the name be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject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.

In addition, the proposed name must be reevaluated 90 days before approval of the NDA, even if the proposed product characteristics as stated in this review are not altered.

## 1 BACKGROUND

### 1.1 INTRODUCTION

This re-review for the proposed name, Samsca, was written in response to a request from the Division of Cardiovascular and Renal Products to rule out any objections to the proposed proprietary name based upon approval of other proprietary or established names from the signature date of the previous DMEPA name review. The Applicant initially proposed a 60 mg strength in addition to the 15 mg and 30 mg strengths; however, they have since withdrawn the 60 mg strength for this NDA submission.

Additionally, revised carton and insert labeling were provided for review and comment.

### 1.2 REGULATORY HISTORY

The Applicant initially submitted Samsca<sup>\*\*\*</sup> as their primary proposed proprietary name for NDA 22-275. DMEPA found the name unacceptable based on [REDACTED]. The secondary name, Samsca, was determined to be acceptable (OSE review #2007-2369 and 2008-787 dated July 18, 2008). However, product characteristics have changed (i.e., no longer marketing 60 mg strength), thus this finding has been rescinded.

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The labels and labeling for this product were also evaluated in OSE review #2007-2369 and 2008-787 dated July 18, 2009. Label and labeling comments will be deferred until the Applicant resubmits revised labels.

Due to the increased risk for osmotic demyelination syndrome (ODS), Samsca must be initiated in the hospital. This restriction has triggered a REMS which includes a Medication Guide, which has been submitted and has undergone review by OSE (OSE review #2008-1857).

### 1.3 PRODUCT INFORMATION

Samsca (Tolvaptan) is a selective vasopressin receptor antagonist that when taken orally, causes an increase in urine excretion that results in an increase in free water clearance (aquaresis), a decrease in urine osmolality and an increase in serum sodium concentrations. Samsca is proposed to be indicated for the treatment of clinically significant hypervolemic and euvoletic hyponatremia (serum sodium < 125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid

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

retention) including patients with heart failure, cirrhosis, and Syndrome of Inappropriate Antidiuretic Hormone (SIADH). Samsca will be available as 15 mg and 30 mg tablets in blisters of 10.

The recommended starting dose is 15 mg once daily. The dose may be increased at intervals  $\geq 24$  hours to 30 mg once daily, and to a maximum of 60 mg once daily as needed to raise serum sodium. During titration, patients should be monitored for serum sodium and volume status. Samsca must be initiated in the hospital.

## 2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary objective for the assessment is to identify and remedy potential sources of medication error prior to drug approval. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>1</sup>

### 2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Samsca, 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.

For the proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see section 2.1.2 for detail) and held a Center of Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see section 2.1.3). DMEPA staff also conducts internal CDER prescription analysis studies. When provided, external prescription analysis studies results are considered and incorporated 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 (see section 2.1.4 for details). The overall risk assessment is based on the findings of a Failure Mode 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.<sup>2</sup> FMEA is used to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed 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 product may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

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

<sup>2</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to established name of the proposed product, proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.<sup>3</sup>

### **2.1.1 Search Criteria**

The DMEPA 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.

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.<sup>4,5</sup>

To identify drug names that may look similar to Samsca, 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 (6 letters), upstrokes (one, capital letter 'S'), downstrokes (none), cross-strokes (none), and dotted letters (none). Additionally, several letters in Samsca may be vulnerable to ambiguity when scripted, including the letter 'S' may appear as 'A', 'L', 'I', 'Z', lower case 'f', 'g', or 'r'; lower case 'a' appears as a lower case 'e', 'n', 'o', 'r', or 'u'; and lower case 'm' may appear as lower case, 'n', 'w', or the letters 'vu'; and lower case 'c' may appear as lower case 'e'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Samsca.

When searching to identify potential names that may sound similar to Samsca, the DMEPA staff search for names with similar number of syllables (two), stresses (SAM-sca or sam-SCA), and placement of vowel and consonant sounds. Additionally, several letters in Samsca may be subject to interpretation when spoken, including the letter 'S' may be interpreted as 'Z'; the letter 'm' may be interpreted as 'n'; or the letter 'c' may be interpreted as 'k' and vice versa. The Applicant's intended pronunciation of the proprietary name was taken into consideration, as this was provided with the proposed name submission. Although the intended pronunciation was provided, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

The DMEPA 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 following information was provided about the proposed product to the medication error staff: proposed proprietary name (Samsca), proposed established name (tolvaptan), proposed indication of use (hyponatremia), strength (15 mg and 30 mg), dose (15 mg to 60 mg), frequency of administration (once daily), route (oral), and dosage form (tablet). Appendix A provides a more detailed listing of the product characteristics the medication error staff general takes into consideration.

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<sup>3</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

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

<sup>5</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

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

### ***2.1.2 Database and Information Sources***

The proposed proprietary name was provided to the DMEPA 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 were not identified in the previous reviews that may sound-alike or look-alike to Samsca using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 6. To complement the process, the medication error staff uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff reviewed the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators were then pooled and presented to the CDER Expert Panel.

### ***2.1.3 CDER Expert Panel Discussion***

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

The pooled results of the DMEPA 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.

### ***2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name***

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode 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.<sup>6</sup> When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed name to be confused with another drug name as a result 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 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

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

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 Samsca 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 Samsca 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 name possesses 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.

DMEPA 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 PROPRIETARY name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and 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 a USAN (United States Adopted Names) stem, particularly in a manner that is contradictory to the USAN Council’s definition.
5. 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.

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 is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proposed 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 (IOM), World Health Organization (WHO), Joint Commission of Accreditation of Hospitals (JCAHO), and the Institute of Safe Medication Practices (ISMP), who 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, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, postmarketing 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 Applicants 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, 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 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 FMEA process is used 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.

### 3 RESULTS

#### 3.1 PROPRIETARY NAME RISK ASSESSMENT

##### 3.1.1 Database and Information Sources

The searches yielded a total of fifteen names as having some similarity to the name Samsca.

Eight of the names were thought to look like Samsca. These names include: Gamene, Simcor, █████, Soma, Sansac, Sumox, Emsam, and █████. Two of the names were thought to sound like Samsca. These names include: SangCya and Sansert. The remaining five names were thought to look and sound similar to Samsca: Samson 8, Zavesca, █████, Samsca<sup>\*\*\*</sup>, and Samska<sup>\*\*\*</sup>.

Additionally, DMEPA did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of February 17, 2009.

##### 3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (see section 3.1.1 above), and noted no additional names thought to have orthographic or phonetic similarity to Samsca.

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

##### 3.1.3 Safety Evaluator Risk Assessment

Since the Applicant will not market a 60 mg tablet, DMEPA re-reviewed all of the twenty-five names identified in the previous OSE reviews (#2007-2369 and 2008-787).

Although the Expert Panel identified 15 names for this review, 11 of these names were previously reviewed in OSE review #2007-2369 and 2008-787. Thus, only 4 new names were identified by the Expert Panel. As such, a total of 29 names were analyzed to determine if the drug names could be confused with Samsca and if the drug name confusion would likely result in a medication error.

Four names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix B). Failure mode and effects analysis (FMEA) was then applied to determine if the potential name, Samsca, could potentially be confused with any of the 25 names and lead to medication errors.

This analysis determined that the name similarity between Samsca and the identified names was unlikely to result in medication errors with any of the 25 products identified for the reasons presented in the Appendices C through H.

### 4 DISCUSSION

#### 4.1 PROPRIETARY NAME RISK ASSESSMENT

Twenty-nine names were evaluated for their potential similarity to the proposed name, Samsca. The FMEA indicates that the proposed name is not likely to result in name confusion that could lead to medication error for the reasons outlined in Appendices B through G.

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

## **5 CONCLUSIONS AND RECOMMENDATIONS**

The Proprietary Name Risk Assessment findings indicate that the proposed name, Samsca, is not vulnerable to name confusion that could lead to medication errors. Thus the Division of Medication Error and Prevention (DMEPA) has no objection to the proprietary name, Samsca, for this product act this time. Additionally, DDMAC does not object to the proposed name, Samsca from a promotional perspective.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product; DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. If the approval of this application is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

### **5.1 COMMENTS TO THE DIVISION**

We would appreciate feedback of the final outcome of this review. We are willing to meet with the Division for further discussion, if needed. Please copy the DMEPA on any communication to the Applicant with regard to this review. If you have any questions or need clarification, contact Sean Bradley, Project Manager, at 301-796-1332.

### **5.2 COMMENTS TO THE APPLICANT**

#### **5.2.1 *Proprietary Name***

We have completed our review of the proposed name, Samsca, and have concluded that it is acceptable. Samsca will be re-reviewed 90 days prior to approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

**Appears This Way  
On Original**

## 6 REFERENCES

### 6.1 REVIEWS

1. OSE Review #2007-2369 and 2008-787, *Proprietary Name, Label and Labeling Review for Samska/Samsca (Tolvaptan) Tablets*, Duffy, F; July 18, 2008.
2. OSE Review #2008-1857, *Review of Patient Labeling (Medication Guide), Carton and Container Labeling, and Medication Guide section of the Risk Evaluation and Mitigation Strategy (REMS), Samsca (Tolvaptan) Tablets*, Mills, Sharon; February 18, 2009.

### 6.2 DATABASES

1. ***Micromedex Integrated Index*** (<http://esilmicromedex.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. ***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 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 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>)

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

**8. *USPTO*** ([www.uspto.gov](http://www.uspto.gov))

USPTO provides information regarding patent and trademarks.

**9. *Clinical Pharmacology Online*** ([www.clinicalpharmacology-ip.com](http://www.clinicalpharmacology-ip.com))

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

**10. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at***  
([www.thomson-thomson.com](http://www.thomson-thomson.com))

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

**11. *Natural Medicines Comprehensive Databases*** ([www.naturalmedicines.com](http://www.naturalmedicines.com))

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

**12. *Stat!Ref*** ([www.statref.com](http://www.statref.com))

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

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

USAN Stems List contains all the recognized USAN stems.

**14. *Red Book Pharmacy's Fundamental Reference***

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

**15. *Lexi-Comp*** ([www.lexi.com](http://www.lexi.com))

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

**16. *Medical Abbreviations Book***

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

**APPENDICES**

**Appendix A:**

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The 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* 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 DMEPA 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). In addition, DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, DMEPA also consider 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		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>

		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	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

**Appendix B:** Names lacking convincing look-alike and/or sound alike similarities with Samsca

Proprietary Name	Similarity to Samsca
Campath	Look and Sound
Zantac	Sound
Septra	Look
SangCya	Look/Sound

**Appendix C:** Proprietary names trademarked in foreign countries by Applicant

Proprietary Name	Similarity to Samsca	Country
Samska	Look and Sound	Canada, Mexico, Japan by Otsuka Pharmaceuticals
Samsca	Look and Sound	Canada, Monaco, Norway, Switzerland, Australia, Japan, South Korea, Liechtenstein

**Appendix D:** Proposed Proprietary name by the Applicant for the same NDA

Proprietary Name	Similarity to Samsca
_____	Look and Sound

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**Appendix E:** Discontinued products with no generics available

Proprietary Name	Similarity to Samsca	Status	Source
Genesa (arbutamine)	Look	Discontinued , no generics available	Drugs@FDA
Sansert (methysergide maleate)	Look/Sound	Discontinued , no generics available	Drugs@FDA

**Appendix F:** Products with no numerical overlap in strength and dose with Samsca

Product name with potential for confusion	Similarity to Samsca	Strength	Usual Dose (if applicable)	Source
Samsca (Tolvaptan) tablets		15 mg, 30 mg	Usual dose: 15 mg to 60 mg once daily (1-2 tabs daily)	Proposed Package Insert
Simcor (Niacin) extended-release/Simvastatin tablets	Look	500 mg/20 mg, 750 mg/20 mg, 1000 mg/20 mg	500 mg-2000 mg niacin extended-release once daily	Facts & Comparisons
Sanctura (Trospium chloride) tablets	Look	20 mg	20 mg twice daily	Facts & Comparisons
Soma (Carisoprodol) tablets	Look	250 mg, 350 mg	250 mg-350 mg three times daily for up to 2-3 weeks	Facts & Comparisons
Sam-e (S-Adenosyl-	Look	200 mg, 400 mg	1-2 tabs one to three times daily	Drugstore.com Facts &

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

Product name with potential for confusion	Similarity to Samsca	Strength	Usual Dose (if applicable)	Source
Samsca (Tolvaptan) tablets		15 mg, 30 mg	Usual dose: 15 mg to 60 mg once daily (1-2 tabs daily)	Proposed Package Insert
Methionine) tablets and extended-release tablets				Comparisons
Sumacal Glucose polymer powder	Look	N/A	Add to food or beverages or mix in water	Facts & Comparisons
Zavesca (Miglustat) capsules	Look/Sound	100 mg	100 mg three times daily	Facts & Comparisons
Samson-8 (Ibuprofen) tablets	Look/Sound	800 mg	400 mg to 800 mg three to four times daily	Clinical Pharmacology.com
Gaviscon (Aluminum hydroxide and Magnesium carbonate) chewable tablets	Look	80 mg, 160 mg	Chew 2-4 tablets four times a day or as directed by physician	Drugstore.com Facts & Comparisons
Senna/Senna-s/Senno Sennoside concentrate tablets	Look	8.6 mg	2 tablets once a day. Maximum of 4 tablets twice a day.	Drugstore.com
Senno Sennoside concentrate tablets	Look	8.6 mg	2 tablets once a day. Maximum of 4 tablets twice a day.	Drugstore.com
Sumox* (Amoxicillin) *Teva no longer uses this proprietary name on its generic product	Look	500 mg cap 125 mg/5 mL	Adults: 500 mg BID or 250 mg TID Peds: 25 mg/kg QD divided Q12 hrs.	Facts & Comparisons

**Appendix G:** Products with no overlap in either strength, dosage form, or route of administration with Samsca

Product name with potential for confusion	Similarity to Samsca	Strength	Dosage Form	Route of administration
Samsca (Tolvaptan)		15 mg, 30 mg	Tablets	Oral
				
Sansac (Erythromycin) Discontinued-generics available	Look and Sound	2%	Solution	Topical
Genasal (Oxymetazoline HCl)	Look	0.05%	Solution	Topical (nasal spray)
Gamene (Lindane) Discontinued-generics available	Look	1%	Shampoo, Lotion	Topical
Zometa (Zoledronic acid)	Look	4 mg/5 mL	Solution	Intravenous
Canasa (Mesalamine)	Look	1000 mg	Suppository	Rectal
Emsam (Selegiline) Extended-release	Look	6 mg/24 hr 9 mg/24 hr 12 mg/24 hr	Transdermal patch	Topical

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**Appendix H:** Potential confusing name with numerical overlap in strength or dose with Samsca

Failure Mode: Name confusion	Causes (could be multiple)	Effects
Samsca (Tolvaptan) tablets	15 mg and 30 mg	Usual dose: 15 mg to 60 mg once daily
Sonata (Zaleplon) capsules	<p>Orthographic similarity ('Sam-' and 'Son-' may appear similar when scripted; both contain 6 letters; both end in '-a')</p> <p>Numerical overlap in strength (5 mg and 15 mg; 10 mg and 15 mg)</p> <p>Overlapping dosage form (solid oral), and route of administration (oral)</p> <p>Achievable overlapping dose (15 mg)</p> <p>Both may be dosed once daily (daily or at bedtime)</p>	<p>Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the endings of the names. Specifically, the letters '-sc-' in Samsca differ from the letters '-at-' in Sonata. The upstroke/cross-stroke 't' in Sonata helps to further differentiate the ending of the name from Samsca, which lacks an upstroke, downstroke, or cross stroke within the name. The additional upstroke 't' at the end of Sonata helps to further differentiate it from Samsca, which only contains one upstroke at the beginning of its name. Thus, the different endings will help to minimize the potential of confusion between Samsca and Sonata.</p> <p>Although both drugs share an overlapping achievable dose, similar numerical strengths, dosing frequency and route of administration, the overall appearance of the names will help to differentiate between them.</p>

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