CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

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

Date:	October 8, 2010
Application Type/Number:	NDA# 201444
Through:	Todd Bridges, RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Denise V. Baugh, PharmD, BCPS, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Nithiodote 1 vial of Sodium Nitrite Injection, USP, 300 mg/10 mL (30 mg/mL) 1 vial of Sodium Thiosulfate Injection, USP, 12.5 grams/50 mL (250 mg/mL)
Applicant:	Hope Pharmaceuticals, Inc.
OSE RCM #:	2010-1360

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

CONTENTS

EXECUTIVE SUMMARY

This review summarizes the Division of Medication Error Prevention and Analysis (DMEPA) proprietary name risk assessment for Nithiodote for co-packaged Sodium Nitrite Injection, USP (30 mg/mL) and Sodium Thiosulfate Injection, USP (250 mg/mL). Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Nithiodote, acceptable for this product (See Section 4 for full discussion). DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the proposed proprietary name, Nithiodote, must be re-evaluated.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Hope Pharmaceuticals, Inc., submitted September 8, 2010, to evaluate the proposed proprietary name, Nithiodote, regarding promotional and potential name confusion with other proprietary or established drug names based on the product characteristics provided by the Applicant.

The Applicant also submitted container labels and carton labeling which will be reviewed under separate cover (OSE Review #2010-1361).

1.2 REGULATORY HISTORY

This NDA is a 505(b)(2) submission for a cyanide antidote containing one vial of sodium nitrite and one vial of sodium thiosulfate. The reference listed drug (RLD) for Nithiodote is sodium thiosulfate injection, USP (NDA # 020166), which was approved on February 14, 1992, (applicant was U.S. Army) to be given with sodium nitrite injection. However, the sodium thiosulfate injection drug product is no longer commercially available and there are no FDA-approved sodium nitrite and sodium thiosulfate products currently marketed in the United States. The only other available treatment for cyanide poisoning is Cyanokit (hydroxocobalamin) for injection (NDA# 022041) which was approved December 15, 2006.

1.3 PRODUCT INFORMATION

Nithiodote, which is indicated for the treatment of [redacted] (b) (4) cyanide poisonings, is composed of one vial of sodium thiosulfate injection and one vial of sodium nitrite injection co-packaged. The proposed dosing regimen is:

1) Inject intravenously 10 mL of a 3% solution (300 mg) of sodium nitrite at the rate of 2.5 to 5 mL/minute. The recommended dose of a 3% solution of sodium nitrite for children is 6 to 8 mL/m^2 of body surface area (approximately 0.2 mL/kg of body weight) not to exceed (NTE) 10 ml of a 3% solution (300 mg).
2) Immediately thereafter, inject 50 mL of a 25% solution (12.5 g) of sodium thiosulfate for adults. The recommended dose of a 25% solution of sodium thiosulfate for children is 30 to 40 mL/m2 of body surface area (approximately 1 mL/kg of body weight) but

dosage should not exceed 50 mL of a 25% solution (12.5 g). The same needle and vein may be used.

Personnel should acquire some skill in the proper method of administering sodium nitrite and sodium thiosulfate prior to an emergency. Cyanide poisoning is fatal.

The patient should be watched closely for at least 24 to 48 hours. If signs of poisoning reappear, one-half of the original doses of both sodium nitrite and sodium thiosulfate should be repeated. Even if the patient seems perfectly well, the medication may be given for prophylactic purposes 2 hours after the first injections. If respiration has ceased but the pulse is palpable, artificial respiration should be applied at once. The purpose is not to revive per se, but to keep the heart beating.

Each carton of Nithiodote consists of:

- one 10 ml glass vial of Sodium Nitrite Injection 30 mg/mL (containing 300 mg of sodium nitrite);
- one 50 mL glass vial of sodium thiosulfate injection 250 mg/mL (containing 12.5 grams of sodium thiosulfate); and
- one package insert.

The kit should be stored at controlled room temperature between 20 C and 25 C (68 F to 77 F); excursions permitted to 15 C to 30 C (59 F to 86 F). Protect from light. Do not permit to freeze.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

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

To identify drug names that may look similar to 'Nithiodote', 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 (ten letters), upstrokes (5, one capital N, two lower case 't', one lower case 'h', and one lower case 'd'), down-strokes (none), dotted letters (2, lower case 'i') and cross-strokes (2, lower case 't'). Additionally, several letters in Nithiodote may be vulnerable to ambiguity when scripted (see Appendix B). As such, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Nithiodote.

When searching to identify potential names that may sound similar to Nithiodote, the DMEPA staff searches for names with similar number of syllables (four), stresses (ni-THI-o-dote,

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

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

or ni-thi-o-DOTE), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary, such as the letters "ni-" which may be interpreted as "ne-", and "thio-" may be interpreted as "thie'-, or "thia-". The Applicant provided their intended pronunciation of the proprietary name, ni/**thī**´-o-dōt\, in the proposed name submission and, therefore, it was taken into consideration. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Nithiodote Prescription Studies (conducted on September 3, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order:  	"nithiodote – use as directed, dispense #1" (pronounced as 'netheeodate')
Outpatient Prescription:  	

2.3 ADVERSE EVENT REPORTING SYSTEM (AERS)

Since sodium thiosulfate has been marketed in the past, DMEPA conducted a search of the Adverse Event Reporting System (AERS) database to identify medication error reports related to the use of this product and thus relevant to this review.

A search was completed on August 18, 2010, without time limitations and used the names, "sodium thiosulfate" and "sodium nitrite" and the verbatim terms "sodium thios%" and "sodium nitri%". The search was conducted using the high level group terms (HLGT) "medication errors" and "product quality issues".

A second AERS search was completed for the marketed product, Cyanokit (hydroxocobalamin) for injection to see if there were any problems with this drug product which could translate to the proposed product, Nithiodote. This search was conducted August 18, 2010, without time restrictions. The product was searched under the names "Cyanokit", "Hydroxocobalamin" and

the verbatim terms “Hydroxoco%” and “Cyanok%” using the high level group terms (HLGT) “medication errors” and “product quality issues”.

3 RESULTS

3.1 DATA BASE AND INFORMATION SOURCES

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

Fourteen of the 18 names (Acetadote, Methadone, Nitrostat, Lithionate, Metadate CD, Metadate ER, Methionine, Nitazoxanide, Nizatidine, Miltefosine, Vilazodone, Nilutamide, Nicorette, and Norethindrone) were thought to look like Nithiodote. One name (Sethotope) was thought to sound like Nithiodote and three names (Methadose, Nithiodote, and Ethiodol) were thought to look and sound like Nithiodote.

A search of the United States Adopted Name stem list on August 26, 2010, did not identify any United States Adopted Names (USAN) stem within the proposed name, Nithiodote.

3.2 CDER EXPERT PANEL DISCUSSION

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

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 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 30 practitioners responded. Four (n = 4) respondents interpreted the name correctly as ‘Nithiodote’, with correct interpretation mostly occurring in the written inpatient studies. The remainder of the responses misinterpreted the drug name. Common misinterpretations included the second ‘i’ mistaken for an ‘r’ and the second ‘o’ mistaken for an ‘a’. Additionally, two respondents in the verbal study misinterpreted the proposed name, Nithiodote, as “Ethiodate”, which is similar to the currently marketed product, Ethiodol. Another respondent in the verbal study misinterpreted the proposed name, Nithiodote, as “Methydate”, which is similar to the currently marketed product, Metadate. Both of these names were identified in our database search and therefore have been included in this review.

3.4 AERS CASES

Both searches did not result in any reports of medication errors that would translate to the use of this drug product, Nithiodote.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified 8 additional names (Menadione, Methimazole, Metaxalone, Metromidol, Naltrexone, Nefazodone, Nutrestore, and MultiHance) thought to look similar to Nithiodote and represent a potential source of drug name confusion.

As such, a total of 26 names were further analyzed to determine if the drug names could be confused with Nithiodote and if the drug name confusion would likely result in a medication error in the usual practice setting. Failure Mode and Effects Analysis was then applied to determine if

the proposed name, Nithiodote, could potentially be confused with any of the 26 names and lead to medication errors.

3.6 COMMENTS FROM THE DIVISION OF ANESTHESIA AND ANALGESIA PRODUCTS (DAAP)

3.6.1 Midpoint of Review

On September 10, 2010, DMEPA notified DAAP via email that we find the name Nithiodote acceptable. Per email correspondence from DAAP on September 10, 2010, they had no objection to the name and did not have any additional comments.

4 DISCUSSION

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

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. The Division of Anesthesia and Analgesia Products and DMEPA concurred with the promotional assessment.

4.2 SAFETY ASSESSMENT

DMEPA identified and evaluated 26 names for their potential similarity to the proposed name, Nithiodote. No other aspects of the name were identified as additional sources of error.

Six of the 26 names were eliminated for the reasons described in Appendices D through G. Specifically, two of the names lacked convincing orthographic and/or phonetic similarities, one name is the subject of this review, one name was unlikely to be written on a prescription, and two products are no longer available and lack a generic equivalent.

Failure Mode and Effects Analysis was applied to determine if the proposed name, Nithiodote, could potentially be confused with the remaining 20 names and lead to medication errors. This analysis determined that the name similarity between Nithiodote and the identified names was unlikely to result in medication errors with any of the 20 products identified for the reasons presented in Appendices H through J.

5 CONCLUSIONS AND RECOMMENDATIONS

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

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. 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. Furthermore, if the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

5.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review. The conclusions upon re-review are subject to change.

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. 3

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. 4 DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

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

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

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

process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

		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

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

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S.

drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

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

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

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

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

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

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

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either

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

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in proposed name, Nithiodote	Scripted may appear as	Spoken may be interpreted as
Capital 'N'	M, VI	N
Lower case 'i'	e, a, l	Any vowel
Lower case 't'	l, f, r	
Lower case 'h'	m, r, u, ls	
Lower case 'i'	e, a, l, r	Any vowel
Lower case 'o'	e, a, u	Any vowel
Lower case 'd'	'cl', 'ci', 'ce'	
Lower case 'o'	e, a, u	Combination letters '-oh-'
Lower case 't'	l, f	
Lower case 'e'	c, i, a	Any vowel

Appendix C: FDA Prescription Study Responses for Nithiodote

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Nithrodote	Nithiodate	Ethiodate
Nithrodote	Nithiodate	Nethealdate
Nithiodate	Nithiodate	Metheodate
Nithiodote	Nithiodate	Nafieldate
Nithiodote	Nithiodate	Methydate (Metadate)
Nithrodote	Nithiodate	Afieldate
Nithiodote	Mithiodate	Ethiodate
Nithriodote	Nithiodate	
Nithiodote	Nithiodate	
Nithrodote	Nithiodate	
Nithrodote		
Nithrodote		
Nithrodote		

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

Proprietary Name	Similarity to Nithiodote
Nitazoxanide	Look
Nicorette	Look

Appendix E: Drug name which is the subject of this review.

Proprietary Name	Source
Nithiodote	SAEGIS, USPTO

Appendix F: Drug name that is unlikely to be written on a prescription

Proprietary Name	Similarity to Nithiodote	Comments
Miltefosine	Look	An oral and topical synthetic ether phospholipid analog (Clin Pharm)

Appendix G: Products no longer available in the marketplace and lacking a generic equivalent.

Proprietary name	Similarity to Nithiodote	Status/Comments
Sethotope (selenomethionine Se-75) injection 85 – 550 uCi/mL NDA# 017047	Sound	A radioactive diagnostic agent; Applicant requested withdrawal of the NDA in correspondence dated February 15, 2007 (per DARRTS)
Menadione (menadione) 5 mg oral tablet NDA# 002139	Look	A precursor to vitamin K3; Applicant withdrew the NDA in 1992

Appendix H: Names of products with no overlap in strength and/or dose and different product characteristics

Product name with potential for confusion	Similarity to proposed proprietary name	Strength	Usual Dose (if applicable)	Other Differentiating Product Characteristics
Nithiodote (Sodium Nitrite and Sodium Thiosulfate) Injection		**300 mg/ 12.5 grams**	**Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**	**Route of administration: intravenous** **Dosage Form: Injection** **Indication: antidote for cyanide poisoning**
Nitrostat (nitroglycerin) sublingual tablet	Look	0.3 mg, 0.4 mg	Take one tablet every 5 minutes, repeat x 3 doses, and call 911	**Route of administration**: oral vs. intravenous **Dosage form**: tablet vs. injection **Product Strength**: Nitrostat is available in multiple strengths which would need to be indicated by the prescriber.
Metadate ER (methylphenidate)	Look	10 mg, 20 mg	Use 'ER' in place of immediate release tablets when the 8 hour dosage of ER corresponds to the titrated 8 hour dosage of immediate release	**Route of administration**: oral vs. intravenous **Dosage form**: tablet vs. injection **Frequency**: every 8 hours vs. one time with repeat dose when indicated **Product Strength**: Metadate is available in multiple strengths which would need to be indicated by the prescriber.

Product name with potential for confusion	Similarity to proposed proprietary name	Strength	Usual Dose (if applicable)	Other Differentiating Product Characteristics
Nithiodote (Sodium Nitrite and Sodium Thiosulfate) Injection		**300 mg/ 12.5 grams**	**Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**	**Route of administration: intravenous** **Dosage Form: Injection** **Indication: antidote for cyanide poisoning**
Methionine capsule or tablet	Look	500 mg	Dietary supplement: 500 mg daily	**Route of administration**: oral vs. intravenous **Dosage form**: tablet/capsule vs. injection **Frequency**: once daily vs. one time with repeat dose when clinically indicated
Methimazole tablet	Look	5 mg, 10 mg	15 mg to 60 mg in 3 divided doses 8 hours apart	**Route of administration**: oral vs. intravenous **Dosage form**: tablet vs. injection **Frequency**: 3 divided doses 8 hours apart vs. one time with repeat dose when indicated **Product Strength**: Methimazole is available in multiple strengths which would need to be indicated by the prescriber.
Vilazodone is the established name for (b) (4)	Look	10 mg, 20 mg, 40 mg	Titrate up from 10 mg per day to to 40 mg once daily	**Route of administration**: oral vs. intravenous **Dosage form**: tablet vs. injection **Frequency**: once daily vs. one time with repeat dose when indicated **Product Strength**: (b) (4) is available in multiple strengths which would need to be indicated by the prescriber.

Appendix I: Drug names with single strength availability but with differentiating product characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Nithiodote (Sodium Nitrite and Sodium Thiosulfate) Injection		**300 mg/ 12.5 grams**	**Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**	
Nilutamide (established name for Nilandron) tablet	Look	150 mg	150 mg once daily	**Route of administration**: oral vs. intravenous **Dosage form**: tablet vs. injection **Frequency**: once daily vs. once with repeat dose when clinically indicated
Metaxalone (established name for Skelaxin) tablet	Look	800 mg	800 mg orally 3 to 4 times daily	**Route of administration**: oral vs. intravenous **Dosage form**: tablet vs. injection **Frequency**: 3 to 4 times daily vs. one time with repeat dose when indicated

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Nithiodote (Sodium Nitrite and Sodium Thiosulfate) Injection		**300 mg/ 12.5 grams**	**Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**	
Nutrestore (glutamine) powder	Look	5 grams per packet	5 grams orally 6 times per day with meal/snack at 2 to 3 hour intervals while awake; treatment can continue for up to 16 weeks	**Route of administration**: oral vs. intravenous **Dosage form**: powder for oral administration vs. solution for intravenous administration **Frequency**: 6 times daily vs. one time with repeat dose when indicated
Norethindrone is the established name for Micronor Tablet Progestin-only oral contraceptive indicated to prevent pregnancy	Look	0.35 mg	One tablet orally once daily	**Route of administration**: oral vs. intravenous **Dosage form**: tablet vs. injection **Frequency**: once daily vs. once with repeat dose when clinically indicated

Appendix J. Potential confusing names with Nithiodote but analysis indicates low potential for confusion.

Proposed name: **Nithiodote** **(Sodium Nitrite and Sodium Thiosulfate) Injection**	**Strength:** **300 mg/12.5 grams**	**Usual Dose:** **Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Ethiodol (ethiodized oil) Contains 37% iodine A sterile, injectable radio-opaque diagnostic agent for use in hysterosalpingography and lymphography.	Orthographic and phonetic similarities stem from sharing the combination letters '-thiodo-' within their names. Shared product characteristics include dosage form (injection), route of administration (intravenous), and frequency of administration (one time)	Confusion leading to medication errors in the usual practice setting is unlikely for the following reasons: *Rationale*: The first letters of this name pair do not look alike when written ('E' vs. 'N'). Additionally, the proposed name, 'Nithiodote' is longer in appearance than 'Ethiodol' when written and the terminal letter 'l' in Ethiodol gives this name a different shape. These features should minimize the potential for confusion orthographically. Phonetically, the suffixes for this name pair do not sound alike. For Ethiodol, the suffix ('dol') may sound like 'dawl' and for Nithiodote, the suffix ('dote') may sound like 'doht'. Furthermore, the dose for these agents differ (*salpinography*: 5 mL initially, then 2 mL increments are injected until tubal patency is established or *lymphography*: 0.1 mL to 0.2 mL per minute vs. 10 mL/50 mL)
Metromidol (metronidazole) tablet 250 mg, 500 mg, 500 mg/100 mL premixed solution for intravenous use The proprietary name, Metromidol, has been discontinued, however, generic equivalents still exist in the marketplace and therefore, Metromidol may be prescribed and substituted with a generic product.	Orthographic similarities stem from the following: similar appearance of their first letter ('M' vs. 'N') when written; sharing some of the same upstrokes (lower case 't') and letter combinations ('-do-') in similar locations (METROMIDOL vs. NITHIODOTE); and an upstroke at or near the end of their names ('l' vs. 't'). All of these shared orthographic features give this name pair a similar shape. Shared product characteristics include dosage form (injection) and, potentially, the route of administration (intravenous).	Confusion leading to medication errors in the usual practice setting is unlikely for the following reasons: *Rationale*: Metromidol (metronidazole) is available in more than one strength and dosage form. Therefore, the prescriber must specify both of these product characteristics in order for the healthcare practitioner to dispense/administer the medication as intended. The frequency of administration for these drug products differ (every 6 to 8 hours vs. one time with a repeat dose if indicated) and Nithiodote is unlikely to be stored in the same area as Metromidol because of its use in a crisis involving cyanide poisoning.

Proposed name: **Nithiodote** **(Sodium Nitrite and Sodium Thiosulfate) Injection**	**Strength:** **300 mg/12.5 grams**	**Usual Dose:** **Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
MultiHance (gadobenate dimeglumine) intravenous injection 529 mg/mL MultiHance is a gadolinium-based contrast agent indicated for intravenous use in magnetic resonance imaging (MRI) of the central nervous system (CNS) in adults and children over 2 years of age The recommended dose is 0.1 mmol/kg (0.2 mL/kg) given as a rapid bolus intravenous injection. To ensure complete injection of the contrast medium, follow the injection with a 5 mL saline flush.	Orthographic similarities stem from the similar appearance of their first letters ('M' vs. 'N'), having two sequential up-strokes ('-lt-' vs. '-th-') in the same position within their names. Shared product characteristics include dosage form (injection) and the route of administration (intravenous) and possibly frequency of administration (one time).	Confusion leading to medication errors in the usual practice setting is unlikely for the following reasons: *Rationale*: The suffixes for these name pair are different when written ('-ance' vs. '-ote') which gives these names different shapes orthographically. Additionally their doses are different (0.2 mL per kilogram vs. 10 mL/50 mL). Additionally, MultiHance and Nithiodote are unlikely to be stored in similar areas of the pharmacy since one is an imaging agent, the other an antidote for cyanide poisoning. Furthermore, the usual practice settings for these agents do not overlap.
Methadone Oral tablet, 5 mg, 10 mg Oral concentrate 10 mg/mL Injection, 10 mg/mL Maintenance treatment of opioid addiction : 80 mg to 120 mg once daily (initial doses may be 20 mg to 30 mg) Pain: 2.5 mg to 10 mg every 8 hours to 12 hours when oral methadone is used as the first analgesic in patients who are not already being treated with and tolerant to opioids	Orthographic similarities stem from the similar appearance of their first letters ('M' vs. 'N') and overlapping positions of their first three upstrokes ('th' and 'd'). Possible overlapping product characteristics include dosage form (injection) and route of administration (intravenous). May have numerical overlap in strength (300 mg) and dose (30 mg)	Confusion leading to medication errors in the usual practice setting is unlikely for the following reasons: *Rationale*: There is a fourth upstroke (the last 't') in Nithiodote which is absent in the name, methadone and this may distinguish these names from each other. Additionally, methadone is available in more than one strength and dosage form. Therefore, a prescriber will have to clarify both in order for the medication to be dispensed/administered as intended.

Proposed name: **Nithiodote** **(Sodium Nitrite and Sodium Thiosulfate) Injection**	**Strength:** **300 mg/12.5 grams**	**Usual Dose:** **Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Methadose (methadone) Oral tablet: 5 mg, 10 mg, 40 mg Oral concentration: 10 mg/mL Maintenance treatment of opioid addiction : 80 mg to 120 mg once daily (initial doses may be 20 mg to 30 mg) Pain: 2.5 mg to 10 mg every 8 hours to 12 hours when oral methadone is used as the first analgesic in patients who are not already being treated with and tolerant to opioids	Orthographic similarities stem from the similar appearance of their first letters ('M' vs. 'N') and overlapping positions of their first three upstrokes ('th' and 'd'). May have numerical overlap in strength (300 mg) and dose (30 mg)	Confusion leading to medication errors in the usual practice setting is unlikely for the following reasons: *Rationale*: There is a fourth upstroke (the last 't') in Nithiodote which is absent in the name, methadone and this may distinguish these names from each other. Additionally, the prescriber will have to clarify the strength for methadose if it is not indicated since the product is available in several strengths. Moreover, the product characteristics for these name pair differ such as dosage form (tablet or oral concentrate vs. injection), and route of administration (oral vs. intravenous).
Nizatidine (established name for Axid) oral capsule, tablet 75 mg, 150 mg, 300 mg 150 mg orally twice daily or 300 mg at bedtime	Orthogradphic similarities stem from having the same first letter ('N') and one upstroke ('d') in the same position. Additionally, this name pair has overlapping strengths (300 mg).	Confusion is unlikely to occur in the usual practice setting. *Rationale*: The name 'Nithiodote' has four upstroke letters within its name vs. two in Nizatidine which gives these names different shapes. Additionally, the dosage forms differ (capsule/tablet vs. injection) and route of administration (oral vs. intravenous).
Acetadote (acetylcysteine) 20% injection 200 mg/mL Usual dose: 300 mg/kg intravenously in divided doses over 21 hours	Orthographic similarity stems from the fact that their suffixes are similar ('adote' vs. 'odote') when written. Shared product characteristics include dosage form (injection) and route of administration (intravenous) as well as their use for an acute exposure to a substance (acetaminophen vs. cyanide). The dose for Acetadote overlaps with the strength for Nithiodote (e.g., 300 mg). Products may be stored in same area of the pharmacy because they are both antidotes.	Confusion between these two names is unlikely to occur in the usual practice setting. *Rationale*: Their prefixes have different appearances when written ('Aceta-' vs. 'Nithio-'). Additionally, their frequencies of administration differ (300 mg/kg intravenously in divided doses over 21 hours vs. one time with a repeat dose if indicated).

Proposed name: **Nithiodote** **(Sodium Nitrite and Sodium Thiosulfate) Injection**	**Strength:** **300 mg/12.5 grams**	**Usual Dose:** **Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Metadate (methylphenidate) CD extended release capsule 10 mg, 20 mg, 30 mg, 50 mg, 60 mg Usual dose: 20 mg once daily in the morning with breakfast; adjust weekly in 10 mg to 20 mg increments up to 60 mg per day	Orthographic similarities stem from similarity of their first letters ('M' vs. 'N') when written and the sharing of upstrokes (two lower case 't's and a lower case 'd') in similar positions within their name. Metadate and Nithiodote have overlapping numerical strengths (300 mg vs 30 mg).	Confusion between these two names is unlikely to occur in the usual practice setting. *Rationale*: The name Nithiodote is longer in appearance than Metadate when scripted. Additionally, the two consecutive upstrokes ('-th-') in Nithiodote form a different shape than that of Metadate giving them different visual appearances. Finally, these products have differing product characteristics such as dosage form (capsule vs. injection) and route of administration (oral vs. intravenous).
Nefazodone tablet 50 mg, 100 mg, 150 mg, 200 mg, 250 mg Usual dose: 100 mg orally twice daily up to a maximum of 600 mg per day	Orthographic similarities stem from sharing the same first letter ('N'), a similar letter combination ('-odo-') in the same position within their names and the same terminal letter ('e'). Nithiodote 300 mg strength may be achieved with Nefazodone 50 mg, 100 mg, and 150 mg strengths.	Confusion between these two names is unlikely to occur in the usual practice setting. *Rationale*: Nithiodote contains two consecutive upstrokes ('-th-') in its prefix and a cross-stroke ('t') in its suffix which gives this name a different shape from the name, Nefazodone. Additionally, this name pair has different product characteristics such as dosage form (tablet vs. injection), route of administration (oral vs. intravenous), and frequency of administration (twice daily vs. one time with repeat dose when indicated).
Naltrexone tablet 50 mg Usual dose: 50 mg orally once daily	Orthographic similarity stems from sharing the same first letter ('N') and consecutive upstrokes in the same position within their names ('-lt-' vs. '-th-'). This name pair have overlapping numerical strengths (50 mg vs. 50 mL)	Confusion between these two names is unlikely to occur in the usual practice setting. *Rationale*: Nithiodote contains two upstrokes (lower case 'd' and 't') in its suffix which gives this name a different shape from Naltrexone. Additionally, this name pair has different product characteristics such as dosage form (tablet vs. injection) and route of administration (oral vs. intravenous).

Proposed name: **Nithiodote** **(Sodium Nitrite and Sodium Thiosulfate) Injection**	**Strength:** **300 mg/12.5 grams**	**Usual Dose:** **Sodium Nitrite 10 mL (0.3 grams) given intravenously over 2 to 4 minutes followed immediately by sodium thiosulfate 50 mL (12.5 grams)**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Lithionate (lithium citrate) oral syrup 8 meq/5 mL (equivalent to the amount of lithium in lithium carbonate 300 mg) Usual dose: 10 mL three times daily for the treatment of acute mania	Orthographic similarity stems from sharing the combination letters '-ithio-' and the suffix '-te'. These products have an overlapping numerical dose (10 mL). As both products are available in single strengths, either may be dispensed as '1' which suggests 1 bottle (for Lithionate) or 1 box (for Nithiodote).	Confusion between these two names is unlikely to occur in the usual practice setting. *Rationale*: The first letters for this name pair do not look alike when scripted ('N' vs. 'L'). Additonally, there is an 'extra' up-stroke ('d') at the beginning of 'Nithiodote' which is absent in Lithionate. This gives the names different shapes. Differing product characteristics include dosage form (syrup vs. injection), route of administration (oral vs. intravenous) and frequency of administration (three times daily vs. one time with repeat dose if needed).

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/s/

DENISE V BAUGH
10/08/2010

TODD D BRIDGES
10/08/2010

DENISE P TOYER
10/08/2010

CAROL A HOLQUIST
10/08/2010