

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-717

PROPRIETARY NAME REVIEW(S)

**Division of Medication Errors and Technical Support
Office of Surveillance and Epidemiology
WO 22, MAIL STOP 4447
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: May 15, 2006

NDA#: 21-717

NAME OF DRUG: **S-Caine**
(Lidocaine and Tetracaine Cream) 7%/7%

NDA SPONSOR: Zars, Inc.

I. INTRODUCTION

This consult was written in response to a request from the Division of Anesthesia, Analgesia, and Rheumatology Products (HFD-170), for an assessment of the proprietary name, S-Caine, regarding potential name confusion with other proprietary or established drug names. The sponsor initially submitted the proprietary name, _____ for review. However, the Division of Drug Marketing, Advertising, and Communications (DDMAC) found the name _____ unacceptable from a promotional perspective and the Division concurred (see OSE Consult #04-0174-1).

Subsequently, DMETS received a request from the Division to re-review the alternate name S-Caine. The name, S-Caine, was previously submitted for the transdermal patch dosage form of this product (NDA #21-623), and reviewed in OSE Consult #03-0263 dated January 14, 2004. DMETS had no objection to the use of the name, S-Caine. However, the sponsor decided not to pursue the use of the name, S-Caine, at that time. Therefore, only S-Caine will be reviewed by DMETS from a safety perspective. Container labels, carton and insert labeling were submitted for review and comment.

PRODUCT INFORMATION

S-Caine is a topical local anesthetic cream consisting of a eutectic mixture of lidocaine 7% and tetracaine 7%. When the cream is applied to the skin, the cream forms a pliable peel. S-Caine is indicated for local dermal anesthesia. For minor dermal procedures, _____ is applied to intact skin for 20 to 30 minutes. Whereas, for major dermal procedures, _____ is applied to intact skin for at least 60 minutes. This product requires refrigeration and will be supplied in 30 gram tubes.

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{i,ii} as well as several FDA databases^{iii,iv} for existing drug names which sound-alike or look-alike to S-Caine to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted^v. The SAEGIS^{vi} Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

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

1. DDMAC has no objections to the proposed proprietary name, S-Caine, from a promotional perspective.
2. The Expert Panel identified three proprietary names which were thought to have the potential for confusion with S-Caine. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.

ⁱ MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

ⁱⁱ Facts and Comparisons, online version, Facts and Comparisons, St. Louis, Missouri.

ⁱⁱⁱ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-05, and the electronic online version of the FDA Orange Book.

^{iv} Phonetic and Orthographic Computer Analysis (POCA)

^v www location <http://www.uspto.gov/tmdb/index.html>.

^{vi} Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

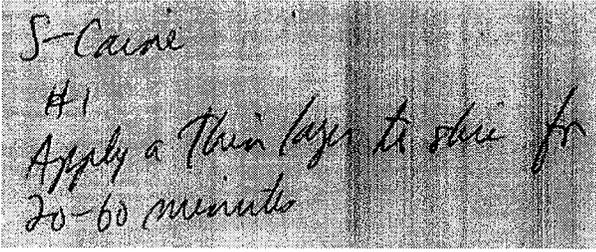
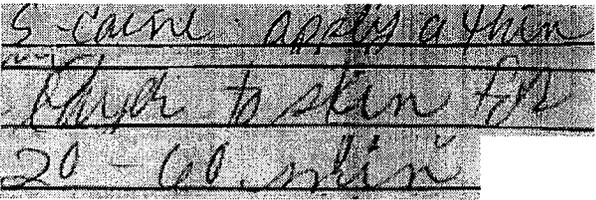
Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Established name, and Dosage form(s)	Usual adult dose*	Other**
S-Caine	Lidocaine and Tetracaine Cream, 70 mg/70 mg	Minor Dermal Procedures: Apply 1 g of S-Caine per 10 cm ² to intact skin for 20 to 30 minutes. Major Dermal Procedures: Apply 1 g of S-Caine per 10 cm ² to intact skin for at least 60 minutes.	
Sensorcaine	Bupivacaine Hydrochloride Injection, 0.25%, 0.5%, 0.75%, 0.25% with 1:200,000 epinephrine, 0.5% with 1:200,000 epinephrine, 0.75% with 1:200,000, 0.75% in 8.25% dextrose	Administration of the smallest dose and concentration required to produce the desired result. This could range from 2 mL to 50 mL or 10 mg to 150 mg of bupivacaine depending upon indication.	LA
Alcaine	Proparacaine Hydrochloride Ophthalmic Solution, 0.5%	For deep anesthesia: Instill 1 drop every 5 to 10 minutes for 5 to 7 doses.	LA
Nesacaine	Chloroprocaine Hydrochloride Injection, 1%, 2% and 3%	Administration of the smallest dose and concentration required to produce the desired result. This could range from 0.5 mL to 40 mL or 10 mg to 800 mg of chloroprocaine depending upon indication.	SA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of S-Caine with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. Each study employed a total of 119 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for S-Caine (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> 	<p>S-Caine quantity 1 apply a thin layer to skin for 20 to 60 minutes.</p>
<p><u>Inpatient RX:</u></p> 	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A (page 9) for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proposed proprietary name “S-Caine”, the primary concerns related to potential look-alike and sound-alike confusion with Sensorcaine, Alcaine, and Nesacaine. Upon further review of the names gathered from EPD, the names Sensorcaine and Alcaine were not reviewed further due to a lack of convincing look-alike similarities in addition to numerous differentiating product characteristics such as the product strength, usual dose, frequency of administration, route of administration, and dosage formulation.

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

1. Sound-Alike Assessment

Nesacaine and the proposed name, S-Caine, have the potential to sound similar when spoken. The second syllable of the name Nesacaine may be indistinguishable since it consists of only one letter (“a”). Thus, if the initial letter “N” of the name Nesacaine is not enunciated clearly and the second syllable is indistinguishable, the name may be misinterpreted as “Es-Caine”. Phonetically, S-Caine is the same as “Es-Caine”. However, because Nesacaine is available in three different strengths (1%, 2%, and 3%), a strength would need to be obtained from the prescriber prior to administering the medication, unlike S-Caine, which is available in only one strength (7%/7%). Additional product characteristics which may also help to distinguish this name pair include route of administration (topical vs. injectable), dosage formulation (cream vs. solution), and unit of measure (gram vs. mL or mg). Furthermore, both products are usually administered by a health professional in a clinic, physician’s office or hospital setting, and not dispensed to patients for administration at home. Due to the above-mentioned differences, DMETS believes the possibility for name confusion between Nesacaine and S-Caine to be minimal.

2. Concerns with Medications Abbreviated as “S-Caine”

The Expert Panel was concerned that the proposed proprietary name, S-Caine, when scripted may look like an abbreviated name. There is a currently marketed anesthetic named Sensorcaine. Thus, it is plausible that a script for S-Caine maybe be misinterpreted as Sensorcaine or some other anesthetic.

DMETS has identified four proprietary names that meet these criteria. This includes the proprietary names Sensorcaine (Rx), Septocaine (Rx), Stypto-Caine (OTC), and Solarcaine (OTC). An Internet search was conducted of three websites, google.com, drugstore.com and destinationrx.com, along with a search of the electronic version of the reference sources Drug Facts and Comparisons and Micromedex Integrated Index to determine if the name “S-Caine” would reference another medication. The searches did not identify an exact match for any medication currently being referenced as “S-Caine” other than the sponsor’s proposed product.

Despite the results from the internet searches, DMETS is unsure if the proprietary name S-Caine is currently used as abbreviation for any of the aforementioned anesthetics. These search results do not take into account abbreviations used in the practice of medicine (e.g., anesthesiology, dentistry). DMETS recommends that the Division request the sponsor conduct independent research on this issue to help ensure there are no currently marketed products being abbreviated as S-Caine. The research should not be limited to searches of reference sources for prescription and over-the-counter products, but should determine if any medications are currently being abbreviated as “S-Caine” in the practice of medicine (e.g., anesthesiology, dentistry, and general medicine).

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of S-Caine, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified several areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. Ensure that the established name is at least one-half the size of the proprietary name in accordance with 21 CFR 201.10(g)(2). Additionally, increase the prominence (i.e., font size) of the product strength commensurate with the proprietary and established name.
2. Relocate the product strength outside of the parentheses which enclose the established name and dosage form. For example,

S-Caine
(Lidocaine and Tetracaine Cream) 7%/7%

3. The lavender ribbon line dissects the primary display panel and it is distracting and definitely more prominent than blue of established name. Moreover, the graphic is more prominent than the drug name and strength.
4. Revise the statement "DOSAGE" TO READ "USUAL DOSAGE".
5. *Detailed* instructions should be provided on how to properly dispose of the peel to prevent accidental application and ingestion by children.

B. CONTAINER LABEL

See GENERAL COMMENTS A1 through A4.

C. CARTON LABELING

1. See GENERAL COMMENTS A1 through A4.
2. Increase the prominence of the "Rx only" and "For topical anesthetic use only." statements.

D. INSTRUCTIONS FOR USE LABELING

1. INSTUCTION #4

See GENERAL COMMENT A5.

2. Delete the use of trailing zeros throughout the insert labeling. FDA will launch a campaign in June 2006, warning health care providers and consumers not to use error-prone abbreviations, acronyms, or symbols (e.g., trailing zeros). Thus, we request that the Divisions not approve or use trailing zeros in their labels and labeling as the potential for a ten-fold dosing error exists if the decimal point is not readily apparent. Additionally, the use of terminal zeroes in the expression of strength or volume is not in accordance with the General Notices (page 10) of 2004 USP, which states, "... to help minimize the possibility of error in the dispensing and administration of the drugs...the quantity of active ingredient when expressed in whole numbers shall be shown without a decimal point that is followed by a terminal zero." We further note that the use of trailing zeros are specifically listed as dangerous abbreviations, acronyms, or symbols in the 2006 National Patient Safety Goals of The Joint Commission for Accreditation of Hospitals (JCAHO). Lastly, safety groups, such as the Institute for Safe Medication Practices (ISMP), also list trailing zeros on their dangerous abbreviations and dose designations list.
3. The #2 step states, "Do not apply near eyes or open wounds". However, it appears from the illustration on the right-hand side that the cream is applied very close to the eyes. Revise the illustration to deter any potential for confusion.

E. INSERT LABELING

1. See GENERAL COMMENT A2.

2. PRECAUTIONS

The information found in the Information for Patients subheading should be repeated at the end of the insert labeling in accordance with 21 CFR 201.57(f)(2).

3. HANDLING AND DISPOSAL

See GENERAL COMMENT A5.

Appendix A. DMETS prescription study results for S-Caine.

Inpatient	Outpatient	Voice
S-caine	S-Caine	Acstain
S-Caine	S-Caine	Actane
S-Caine	S-Caine	Asatane
S-Caine	S-caine	Asatane
S-caine	S-Caine	Ascaine
S-caine	S-Caine	Ascane
S-caine	S-Caine	Ascane
S-caine	S-Caine	Azecaine
S-caint	S-Caine	S-Caine
S-carne	S-Caine	
S-Carne	S-Caine	
S-caine	S-caine	
	S-Caine	

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

/s/

Todd Bridges
6/13/2006 08:49:10 AM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
6/13/2006 08:58:13 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
6/13/2006 09:29:11 AM
DRUG SAFETY OFFICE REVIEWER

CONSULTATION RESPONSE
Division of Medication Errors and Technical Support
Office of Drug Safety
(DMETS; HFD-420)

DATE RECEIVED:
June 10, 2004

DESIRED COMPLETION DATE: August 9, 2004
PDUFA DATE: September 17, 2004

ODS CONSULT #:
04-0174

TO: Bob Rappaport, M.D.
Director, Division of Anesthetic, Critical Care, and Addiction Drug Products
HFD-170

THROUGH: Pratibha Rana
Project Manager, Division of Anesthetic, Critical Care, and Addiction Drug Products
HFD-170

PRODUCT NAME:
TetraPeel
(Lidocaine and Tetracaine Cream)
7%/7%

NDA SPONSOR:
Zars, Inc.

NDA#: 21-717

SAFETY EVALUATOR: Scott Dallas, R.Ph.

RECOMMENDATIONS:

1. Although DMETS has no concerns relating to look-alike and/or sound-alike confusion with the proprietary name TetraPeel, DMETS believes the name TetraPeel is misleading to patients and healthcare professionals since the name implies that the product only contains the anesthetic agent tetracaine, and thus does not recommend the use of the name. DMETS believes the safest use of this product may be best managed under the same proprietary name as NDA 21-623, S-Caine™ Patch (lidocaine and tetracaine topical patch) 70 mg/70 mg.
2. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name TetraPeel acceptable from a promotional perspective. However, DDMAC commented that the name "TetraPeel" alludes to a single active ingredient (tetracaine) as opposed to a combination product of tetracaine and lidocaine.

Carol Holquist, R.Ph.
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**Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Building Room 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: August 10, 2004

NDA NUMBER: 21-717

NAME OF PRODUCT: TetraPeel
(Lidocaine and Tetracaine Cream)
7%/7%

NDA SPONSOR: Zars, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anesthetic, Critical Care and Addiction Drug Products (HFD-170) for an assessment of the proposed proprietary name, TetraPeel, regarding potential name confusion with other proprietary or established names. Draft container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

TetraPeel is a topical local anesthetic cream consisting of a eutectic mixture of lidocaine 7 % and tetracaine 7%. When the cream is applied to the skin, the cream forms a pliable peel. TetraPeel is indicated as a topical local anesthetic for local dermal anesthesia. For minor dermal procedures, _____ should be applied to intact skin for 20 to 30 minutes. Whereas, for major dermal procedures, _____ of TetraPeel _____ should be applied to intact skin for at least 60 minutes. The product is required to be stored in a refrigerator and will be available in a 30 gram tube.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases³ for existing drug names which sound-alike or look-alike to TetraPeel to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's

¹ MICROMEDEX Integrated Index, 2004, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, 2004, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System (DSS), the DMETS database of proprietary name consultation requests (ACCESS), New Drug Approvals 98-04, and the electronic online version of the FDA Orange Book.

trademark electronic search system (TESS) was conducted⁴. The Saegis⁵ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three pharmacy requisition analysis studies consisting of two written pharmacy requisition studies and one verbal requisition study, involving health care practitioners within FDA. This exercise was conducted to simulate the requisition ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

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

1. DDMAC finds the proprietary name TetraPeel acceptable from a promotional perspective. However, DDMAC commented that the name "TetraPeel" alludes to a single active ingredient (tetracaine) as opposed to a combination product of tetracaine and lidocaine.
2. The Expert Panel identified three proprietary names that were thought to have the potential for confusion with "TetraPeel". These products are listed in Table 1 (see below), along with the dosage form available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Established name, Dosage form(s), and Strength(s)	Usual adult dose*	Other**
TetraPeel	Lidocaine and Tetracaine, Cream, 7%/7%	Apply 0.5 g to 1 g of TetraPeel per 10 cm ² to intact skin for 20 to greater than 60 minutes. Dose and time duration depends upon the type of dermal procedure.	
Tetrachel	Tetracycline Hydrochloride, Capsules, 250 mg and 500 mg	Take 1 to 2 g per day orally in 2 to 4 divided doses.	SA/LA
Testopel	Testosterone, Pellets, 75 mg	Inject 150 to 600 mg (2 to 6 pellets) subcutaneously every 3 to 6 months.	SA/LA
Telepaque	Iopanic Acid, Tablets, 500 mg	Take 3 g or 6 tablets orally on two consecutive evenings prior to cholecystography.	LA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

⁴ Website location <http://tess2.uspto.gov/bin/gate.exe?f=tess&state=7cljht.1.1>

⁵ Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. The Expert Panel (EPD) discussed all names considered to have significant phonetic or orthographic similarities to TetraPeel. A search of POCA did not identify any additional names of concern that were not discussed in EPD.

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary names to determine the degree of confusion of "TetraPeel" with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 124 health care professionals (pharmacists, physicians, and nurses) for each proposed proprietary name. These exercises were conducted in an attempt to simulate the prescription ordering process. Two pharmacy requisitions were written, each consisting of a combination of marketed and unapproved drug products and included a requisition for TetraPeel (see page 5). These requisitions were optically scanned and one requisition was delivered to a random sample of the participating health professionals via email. In addition, a pharmacy requisition was recorded on voice mail and included an order for TetraPeel. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal pharmacy requisitions, the participants sent their interpretations of the products via e-mail to the medication error staff.

HANDWRITTEN PHARMACY REQUISITIONS			VERBAL PHARMACY REQUISITION:									
<p>Sample 1:</p> <table border="1"> <thead> <tr> <th>#</th> <th>ORDER Code</th> <th>ITEM (include strength and size)</th> </tr> </thead> <tbody> <tr> <td>1cs</td> <td>44BR</td> <td>DSW 100ml</td> </tr> <tr> <td>6</td> <td>351J</td> <td>TetraPeel</td> </tr> </tbody> </table>			#	ORDER Code	ITEM (include strength and size)	1cs	44BR	DSW 100ml	6	351J	TetraPeel	<p>TetraPeel Quantity of Six</p>
#	ORDER Code	ITEM (include strength and size)										
1cs	44BR	DSW 100ml										
6	351J	TetraPeel										
<p>Sample 2:</p> <table border="1"> <thead> <tr> <th>#</th> <th>ORDER Code</th> <th>ITEM (include strength and size)</th> </tr> </thead> <tbody> <tr> <td>1cs</td> <td>44BR</td> <td>DSW 100ml</td> </tr> <tr> <td>6</td> <td>351J</td> <td>TetraPeel</td> </tr> </tbody> </table>			#	ORDER Code	ITEM (include strength and size)	1cs	44BR	DSW 100ml	6	351J	TetraPeel	
#	ORDER Code	ITEM (include strength and size)										
1cs	44BR	DSW 100ml										
6	351J	TetraPeel										

2. Results:

One participant in the verbal pharmacy requisition study interpreted the proposed name as Tetrafil. A search of the online version of Micromedex referenced

Tetrafil as the active ingredient tetracycline. However, an online search of the Orange Book, Stat Ref, Clinical Pharmacology, Drug Facts and Comparison, and the U.S. Patent and Trademark Office, and a bound version of the 2003 Red Book did not identify the name Tetrafil as a proprietary name for a tetracycline product. See Attachment A for the complete listing of interpretations from the verbal and written prescription studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

1. Look-alike and Sound-alike Concerns with TetraPeel

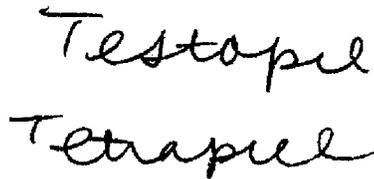
In reviewing the proposed proprietary name “TetraPeel”, the primary concerns related to the potential for look-alike and sound-alike confusion with Tetrachel, Testopel and Telepaque.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that the proposed name, TetraPeel, could be confused with the name Tetrafil. One respondent from the verbal pharmacy requisition study misinterpreted the name, TetraPeel, for the name Tetrafil. The name Tetrafil was referenced in the online version of Micromedex to identify the active ingredient tetracycline. Although there are limitations to the predictive value of these studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretation with this drug product. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population. However, if a healthcare worker initially interpreted the name as Tetrafil and assumed it was a generic formulation of a tetracycline product, then numerous product characteristic differences should alert the healthcare worker that the interpretation of the name as a tetracycline product was in error. Tetrapeel and tetracycline products differ in their product strengths, indications of use, frequency of administration, route of administration, dosage formulation, and duration of therapy.

- a. Tetrachel was identified to have look-alike and sound-alike similarities to the proposed name, TetraPeel, when scripted and spoken. The only difference between the names is the sixth and seventh letters, “ch” vs. “Pe”. Therefore, these letters must be clearly scripted to differentiate the names when written, and when spoken the “ch” and “p” must be clearly enunciated. An online search of the Orange Book and Martindale’s in MicroMedex Integrated Index indicates that the product Tetrachel has been discontinued in United States and in foreign markets. However, a healthcare worker could initially interpret the name as Tetrachel and assume the physician wanted a generic version of tetracycline. However, these products differ in their product strength (250 mg and 500 mg vs. 7%/7%), indication of use (to treat systemic infections vs. local dermal anesthesia), frequency of administration (2 to 4 times a day vs. a one time application), route of administration (oral vs. topical), dosage formulation (capsule vs. cream) and duration of therapy (continuous use for 7 days or longer vs. intermittent use or a one time application). Although these names possess look and sound-alike similarities, the many aforementioned product differences decrease the likelihood of confusion or medication errors between the two products.



- b. Testopel was identified to have look-alike and sound-alike similarities to the proposed name, TetraPeel. If TetraPeel were scripted with a lower case letter “p”, then it would increase the look-alike similarity between the names. The orthographic similarity would be a result of the upstroke from the second letter “t”, followed by a downstroke from the letter “p”, and ending with an upstroke from the letter “l”. Also both names would appear to have a similar length when scripted. Both names consist of three syllables of similar length when spoken, and each syllable begins with the same corresponding letter/sound. These features can cause the names to possess a rhyming quality and thus sound similar when spoken. However, these products differ in their product strength (75 mg vs. 7%/7%), indication of use (androgen replacement therapy vs. local dermal anesthesia), usual dose (2 to 6 pellets vs. 0.5 g to 1 g), route of administration (subcutaneous vs. topical), dosage formulation (pellet vs. cream), and package configuration (one pellet per vial vs. tube). Testopel is classified as a schedule C-III controlled substance. This medication would generally only be administered by a trained healthcare professional, who would be monitoring the patient’s response to the androgen replacement therapy. Although these names possess look and sound-alike similarities, the many aforementioned product differences decrease the likelihood of confusion or medication errors between the two products.



- c. Telepaque was identified to have look-alike similarities to the proposed name, TetraPeel. Both names consist of 9 letters, and begin with the letters “Te”. If TetraPeel were scripted with a lower case letter “p”, then both names would feature an upstroke in the third position “l” vs. “t”, followed by a downstroke from the letter “p”. However, the names do possess some features that can differentiate the names when scripted. For example, the name Telepaque can possess an additional downstroke from the letter “q”, whereas the name TetraPeel can possess an additional upstroke from the last letter “l”. Also the last four letters after the letter “p” in Telepaque can appear longer in length than the last three letters after the letter “p” in TetraPeel. These products differ in their product strength (500 mg vs. 7%/7%), indication of use (oral cholecystography vs. local dermal anesthesia), usual dosage (3 g or 6 tablets vs. 0.5 g to 1 g), route of administration (oral vs. topical), and dosage formulation (tablet vs. cream). The differences in the packaging configurations could also aid in differentiating the scripted name on an outpatient prescription. Since the quantity to be dispensed on a prescription for Telepaque

would commonly be scripted as #6 or #12 tablets, whereas the quantity to be dispensed on a prescription for TetraPeel would commonly be scripted as 1 tube or 30 g. Although these names possess some look-alike similarities, the aforementioned product differences decrease the likelihood of confusion or medication errors between the two products.



The image shows two lines of handwritten text in cursive. The top line reads 'Tetrapone' and the bottom line reads 'TetraPeel'. The letters are slanted and connected, making them difficult to distinguish at a glance.

2. Other safety concerns with the name, TetraPeel

The sponsor has combined the prefix “tetra” and word “peel” to create the name TetraPeel. Capitalizing the letter “p” emphasizes that the name consists of two distinct parts, “Tetra” and “Peel”. DMETS believes that by presenting the name in this manner implies that the product only contains the anesthetic tetracaine that forms a pliable peel when applied to the skin.

The name does not suggest that the product also contains an equal concentration of the anesthetic agent, lidocaine. Therefore, DMETS is concerned that patients and healthcare professionals may not be cognizant of the fact that the product contains a 7% concentration of lidocaine. Since tetracaine is systemically absorbed less than lidocaine, DMETS questions if the name TetraPeel may also imply to healthcare professionals that the product, TetraPeel, is safer than other anesthetic creams.

DMETS and DDMAC believe the name TetraPeel is misleading to patients and healthcare professionals since the name implies that the product only contains the anesthetic agent tetracaine.

3. Dual Tradenames, NDA 21-623 vs. NDA 21-717

The sponsor, Zars, Inc., has recently received an approvable letter for NDA 21-623. NDA 21-623 is for a topical patch containing 70 mg of lidocaine and 70 mg of tetracaine for local dermal anesthesia. Whereas, NDA 21-717 is for a topical cream and each gram contains 70 mg of lidocaine and 70 mg of tetracaine for local dermal anesthesia. The approvable letter for NDA 21-623 includes the proprietary name of S-Caine™ Patch. The sponsor may begin promoting this product with the proprietary name to healthcare professionals, and inform healthcare professionals the product contains lidocaine and tetracaine.

Therefore, DMETS considers NDA 21-717 as a product line extension of the S-Caine Patch, since it contains the same active ingredients with similar indications of use, local dermal anesthesia. If both dosage formulations utilize the same tradename, then this should aid healthcare professionals to remember that both products contain the same active ingredients, lidocaine and tetracaine, whereas the name TetraPeel only implies one of those ingredients. Therefore, DMETS believes the safest use of this product may be best managed under the same proprietary name as NDA 21-623, S-Caine™ Patch (lidocaine and tetracaine topical patch) 70 mg/70 mg.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of TetraPeel, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL

1. DMETS is unsure if the sponsor is planning to present the proprietary name with the same print color, size, and font as the current presentation of the word "Tradename". Therefore, the sponsor should ensure the established name appears with at least $\frac{1}{2}$ the prominence of the proprietary name based upon print size, color and font.
2. The established name should be presented as "Lidocaine and Tetracaine Cream" and the product strength, 7%/7%, should appear directly below or juxtapose to the established name.
3. DMETS recommends that the net quantity statement, "Net Wt. 30g", be relocated to appear on the principal display panel. However, please ensure the net quantity statement is not relocated in close proximity and has less prominence than the statement of product strength.
4. DMETS recommends increasing the prominence of the route of administration statement and relocating the statement to the principal display panel.
5. DMETS suggests that the "Rx only" statement should be relocated to the principal display panel.
6. DMETS recommends increasing the prominence of the storage condition statement.

B. CARTON LABELING

Refer to comments A1, A2, and A4-A6.

C. INSERT LABELING

1. Refer to comments A1 and A2.

2.

3.

Also all terminal zeros should be deleted when expressing a product strength or quantity. For example, the

designation "1.0 g" should be changed to read "1 g". Please revise.

4. In the "Handling and Disposal" section, DMETS recommends increasing the prominence of the immediate disposal statement. Also include acceptable methods of disposal (i.e., disposal of the used peel in a toilet).

IV. RECOMMENDATIONS:

1. Although DMETS has no concerns relating to look-alike and/or sound-alike confusion with the proprietary name TetraPeel, DMETS believes the name TetraPeel is misleading to patients and healthcare professionals since the name implies that the product only contains the anesthetic agent tetracaine, and thus does not recommend the use of the name. DMETS believes the safest use of this product may be best managed under the same proprietary name as NDA 21-623, S-Caine™ Patch (lidocaine and tetracaine topical patch) 70 mg/70 mg.
2. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.
3. DDMAC finds the proprietary name TetraPeel acceptable from a promotional perspective. However, DDMAC commented that the name "TetraPeel" alludes to a single active ingredient (tetracaine) as opposed to a combination product of tetracaine and lidocaine.

DMETS would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

Scott Dallas, R.Ph.
Safety Evaluator
Office of Drug Safety (DMETS)

Concur:

Denise Toyer, Pharm.D.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Attachment A:

Pharmacy Requisition Studies for TetraPeel

Written Requisition Sample 1	Written Requisition Sample 2	Verbal Requisition
Tetrabell	TetraPeel	Tetrafil
Tetraped	TetraPeel	Tetrapeal
Tetrapeel	TetraPeel	Tetrapeal
Tetrapeel	Tetrapeel	Tetrapeel
Tetrapell	TetraPeel	Tetra-Peel
Tetrapell	Tetrapeel	Tetrapil
Tetrapell	TetraPeel	Tetropeel
Tetrapell	TetraPeel	tetropel
	Tetrapeel	
	TetraPeel	
	TetraPeel	

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/s/

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8/24/04 12:17:17 PM
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