CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-586

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED:	**DESIRED COMPLETION DATE:**	**ODS CONSULT #:**
April 1, 2004	June 18, 2004	04-0129

TO: Janice Soreth, M.D.,
Director, Division of Anti-Infective Drug Products
HFD-520

THROUGH: Maureen Dillon-Parker
Project Manager, Division of Anti-Infective Drug Products
HFD-520

PRODUCT NAME:	**NDA SPONSOR:** 3M Health Care Markets
Duraprep™ Surgical Solution [Iodophor (0.7% available iodine) and Isopropyl Alcohol (74% w/w) Topical Solution] NDA#: 21-586	

SAFETY EVALUATOR: Charlie Hoppes, R.Ph., M.P.H.

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, DuraPrep™. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.

2. Labels and labeling associated with the name DuraPrep™ will be reviewed as a separate consult (ODS Consult #03-0230-1). Comments will be forwarded to the Division in June of 2004.

3. DDMAC finds the proprietary name DuraPrep™ acceptable from a promotional perspective.

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Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: June 1, 2004

NDA# 21-586

NAME OF DRUG: **Duraprep™ Surgical Solution** [Iodophor (0.7% available iodine) and Isopropyl Alcohol (74% w/w) Topical Solution]

NDA HOLDER: 3M Health Care Markets

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anti-Infective Drug Products (HFD-520), for assessment of the proprietary name DuraPrep regarding potential name confusion with other proprietary or established drug names. Container labels and carton labeling were provided for review and comment. However, due to the complexity of this review, comments pertaining to the labels and labeling will be provided in a separate consult from DMETS (ODS #03-0230-1).

DuraPrep™ has been available as an over-the-counter product in the marketplace since 1988, under IND 49,411. In order to comply with the tentative final monograph for topical antiseptic products once it is finalized, the sponsor has filed a new drug application, NDA 21-586. DuraPrep™ has had a history of product safety problems related to the ignition of flammable ingredients upon use. Therefore, DMETS is currently reviewing DuraPrep™ packaging, labels, labeling, and product information from a safety perspective separate from this proprietary name review under a separate consult, ODS# 03-0230-1.

PRODUCT INFORMATION

DuraPrep™ is the proposed proprietary name for Iodophor (0.7% available iodine) and Isopropyl Alcohol (74% w/w) Topical Solution. DuraPrep™ is a film-forming iodophor complex for preparation of the skin prior to surgery. It helps reduce bacteria that potentially can cause skin infection. DuraPrep™ is available over-the-counter in a sterile 6 mL or 26 mL applicator with a urethane sponge tip.

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 databases[3] for existing drug names which

[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, Facts and Comparisons, St. Louis, MO.

sound-alike or look-alike to DuraPrep 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[4]. The Saegis[5] 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 (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name DuraPrep. Potential concerns regarding drug marketing and promotion related to the proposed name was 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 Duraprep acceptable from a promotional perspective.

2. The Expert Panel identified three proprietary names that were thought to have the potential for confusion with DuraPrep. These products are listed in Table 1 (below), along with the dosage forms available and usual dosage. In addition, expert panel members discussed possibilities of confusion between DuraPrep and terms such as "epidural".

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

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
DuraPrep	Iodophor (0.7% available iodine) and Isopropyl Alcohol (74% w/w) Topical Solution	Apply as directed prior to preparation of the skin for surgery.	
Duricef	Cefadroxil Tablets USP, 1 gram Cefadroxil Capsules USP, 500 mg Cephadroxil for Oral Suspension USP, 125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL (when reconstituted)	One or two grams a day in a single or two divided doses.	SA
OraPred	Prednisolone Sodium Phosphate Oral Solution 15 mg (prednisolone)/5 mL	5 mL to 60 mL (5 mg to 60 mg base) per day.	SA
Daraprim	Pyrimethamine Tablets, 25 mg	Take one tablet daily for malaria treatment. Take two to three tablets daily for toxoplasmosis treatment. Take one tablet once weekly for prophylaxis of malaria.	LA

[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-04, and the electronic online version of the FDA Orange Book.

[4] WWW location http://www.uspto.gov/tmdb/index.html.

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

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
DuraPrep	Iodophor (0.7% available iodine) and Isopropyl Alcohol (74% w/w) Topical Solution	Apply as directed prior to preparation of the skin for surgery.	

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)

Appears This Way
On Original

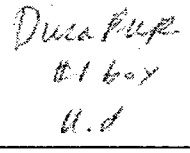
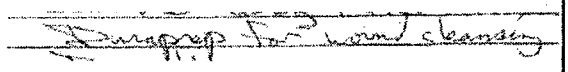
B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

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. No additional names of concern were identified in POCA 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 name to determine the degree of confusion of DuraPrep 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). 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 DuraPrep (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: 	Duraprep Give one box As directed.
Inpatient RX: 	

2. Results:

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

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name DuraPrep, the primary concerns related to the potential for look-alike and sound-alike confusion with Duricef, Orapred, and Daraprim.

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. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, DuraPrep. 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.

Additionally, since DuraPrep™ has been available as an over-the-counter product in the marketplace since 1988, DMETS conducted searches of postmarketing information to determine whether there have been medication errors as a result of confusion with the proprietary name, DuraPrep. A search of the FDA Adverse Event Reporting System (AERS) was conducted. The MedDRA Preferred Terms (PTs), "Medication Error", "Accidental Overdose", "Overdose", "Pharmaceutical Product Complaint", and "Treatment Non-Compliance", and the drug names, "Dura prep%", "Duraprep%", and "Dura-prep%", were used to perform the search. This search strategy returned no reports from AERS. The technical support staff in DMETS provided additional postmarketing information from a broader search of AERS and from the Drug Quality Reporting System (DQRS). These searches yielded ten reports of actual accidents involving the ignition, primarily via cauterization, of DuraPrep, and one report of the potential for this to happen, citing inconspicuous warning statements in the product labeling. Safety-related issues involving reports of ignition of DuraPrep will be addressed in a separate consult from DMETS, ODS Consult #03-0230-1.

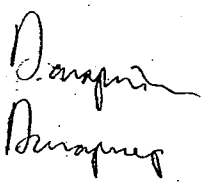
1. Duricef sounds like DuraPrep when spoken. Duricef is the cephalosporin antibiotic cefadroxil, available in tablets, capsules, and powder for oral suspension. Duricef is indicated for urinary tract infections, skin and skin structure infections, and pharyngitis and tonsillitis by susceptible strains. The usual adult dose of Duricef is one or two grams per day in a single or two divided doses. Phonetic similarities between Duricef and DuraPrep are mainly attributed to the first two syllables, "Duri" vs. "Dura", for these three-syllable names. The first two syllables sound especially alike when the "i" in "Duri" and the "a" in "Dura" are pronounced as a short vowel sounds. The last syllable of each name are somewhat distinctive, however, and may serve to differentiate the names phonetically. Although Duricef may sound similar to DuraPrep, there are many differences which may serve to distinguish these products in the marketplace including, dosage form (tablet, capsule, and powder for oral suspension vs. topical solution), route of administration (oral vs. topical), and strength (125 mg, 250 mg, 500 mg, and 1 gram vs. 0.7% iodine/74% w/w isopropyl alcohol), respectively. Because of these differences, lack of convincing sound-alike properties, and absence of documented errors between these products in the marketplace, DMETS considers the likelihood of medication errors resulting from confusion between these products to be low.

2. OraPred may sound like DuraPrep when spoken. OraPred is prednisolone sodium phosphate oral solution an oral steroid for use against inflammation or in acute

exacerbations of multiple sclerosis. Phonetic similarities between OraPred and DuraPrep may be attributed to similarities in the first two syllables, "Ora" vs. "Dura", especially if the "D" in "Dura" lacks emphasis when spoken. The last syllable of each name, "Pred" vs. "Prep", may also sound-alike. Although Orapred may sound similar to DuraPrep, there are many differences that may serve to distinguish these products in the marketplace including, route of administration (oral vs. topical), packaging (237 mL bottle vs. 6 mL or 26 mL applicator bottle with urethane sponge top), usual dosage (5 mL to 60 mL in a single dose daily vs. apply as directed prior to preparation of the skin for surgery), and strength (15 mg prednisolone/5 mL vs. 0.7% iodine/74% w/w isopropyl alcohol), respectively. Because of these differences and absence of documented errors between these products in the marketplace, DMETS considers the likelihood of medication errors resulting from confusion between these products to be low.

3. Daraprim may look like DuraPrep when written. Daraprim is pyrimethamine, an antiparasitic compound available in tablet form for oral administration. Daraprim is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, for the treatment of acute malaria, and for the chemoprophylaxis of malaria due to susceptible strains of plasmodia. Daraprim is available as white, scored tablets containing 25 mg pyrimethamine, in bottles of 100 tablets. Orthographic similarities between Daraprim and DuraPrep may be attributed to the shared letters and their relative placement in each of the names, especially when the initial "P" in DuraPrep is scripted in lower case (see below).

The initial "a" in Daraprim may also look like the "u" in DuraPrep. However, the terminal "p" in DuraPrep may serve to differentiate the name pair orthographically (see writing sample below).



Although Daraprim may look similar to DuraPrep, there are many differences which may serve to distinguish these products in the marketplace including, route of administration (oral vs. topical), dosage form (tablet vs. topical solution), and strength (25 mg vs. 0.7% iodine/74% w/w isopropyl alcohol), respectively. Because of these differences and absence of documented errors between these products in the marketplace, DMETS considers the likelihood of medication errors resulting from confusion between these products to be low.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

Although the sponsor submitted container labels and carton labeling for DuraPrep™, DMETS will address this labeling as well as issues relating to the safe use of this product in a separate consult, ODS Consult #03-0230-1.

IV. RECOMMENDATIONS:

A. DMETS has no objections to the use of the proprietary name DuraPrep™. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.

B. Labels and labeling associated with the name DuraPrep™ will be reviewed as a separate consult (ODS Consult #03-0230-1). Comments will be forwarded to the Division in June of 2004.

C. DDMAC finds the proprietary name DuraPrep™ acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-2102.

Charlie Hoppes, RPh, MPH
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, RPh
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A. Prescription Studies for DuraPrep

Verbal	Inpatient	Outpatient
Duraprep	Duraprep	DuraPrep
Duraprep	Duraprep	DuraPur
Duraprep	Duraprep	Dura Prep
Duraprep	Duraprep	Durapur
Duraprep	DuraPrep	Dura Prep
Duraprep	Duraprep	Dura Pup
Duraprep	Duraprep	Dura Prik
Durapref	Duraprep	Duraprep
Duraprep	Duraprep	Dura Prep
DuraPrep	Duraprep	Dura Prep
Duraprep	Duraprep	Durapup
Duraperp	Duraprep	DuraPur
Duraprep	Duraprep	DuraPur
Duraprep	Duraprep	Dura Prep
Doraprep	Duraprep	Dura Prep
Duraprep	Duraprep	DuraPrep
Duraprep	Duraprep	DuraPak
Duraprep	Duraprep	DucaPUR
Deraprep	Duraprep	Dura Prep
Duraprep	Duraprep	
Duraprep	Duraprep	
	Duroprep	

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