

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*

**21-852**

**PROPRIETARY NAME REVIEW(S)**

**Division of Medication Errors and Technical Support (DMETS)**  
**Office of Drug Safety**  
**HFD-420; White Oak 22, Mail Stop 4447**  
**Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** November 16, 2005

**NDA#:** 21-852

**NAME OF DRUG:** \_\_\_\_\_ (Calcipotriene and Betamethasone Ointment) 0.005%  
\_\_\_\_\_ alternate)  
Taclonex (alternate)

**NDA HOLDER:** LEO Pharmaceutical Products Ltd.

**I. INTRODUCTION:**

This consult was written in response to a request from the Division of Dermatology and Dental Products (HFD-540), to reconsider the acceptability of the proprietary name, Dovobet®, based on the Sponsor's rebuttal submission dated September 16, 2005. DMETS reviewed the proposed proprietary name Dovobet in ODS Consult # 05-0123, dated August 28, 2005. DMETS did not recommend use of the proprietary name, Dovobet due to its potential look-alike and sound-alike similarities to Dovonex.

The Sponsor has proposed to modify the appearance of the tradename to \_\_\_\_\_ to help differentiate it orthographically from Dovonex. However, should the Agency continue to recommend against the tradename, \_\_\_\_\_ the Sponsor has submitted an alternate proprietary name, \_\_\_\_\_, for assessment. The Sponsor has included a proprietary name safety assessment from the Drug Safety Institute, Inc. for the alternate proprietary name, \_\_\_\_\_. Additionally, in the event that neither preferred name is selected \_\_\_\_\_ the Sponsor has submitted the proprietary name of Taclonex.

**PRODUCT INFORMATION**

Dovobet is a topical vitamin D analogue/corticosteroid combination ointment indicated for the topical treatment of psoriasis vulgaris. Dovobet should be applied to affected areas once daily. Dovobet is supplied in 15 gram, 30 gram, 60 gram, and \_\_\_\_\_ gram collapsible tubes. Dovobet is currently marketed in Canada, Ireland, Italy, the Netherlands, and the United Kingdom with the same indication and strength.

**II. RISK ASSESSMENT:**

**A. RECONSIDERATION OF DOVOBET**

The sponsor has requested a re-consideration of the proprietary name, Dovobet, for Calcipotriene 0.005% and Betamethasone \_\_\_\_\_ Ointment. The Sponsor believes the potential for confusion between Dovobet and Dovonex is low for the following reasons (the sponsor's comments are italicized.)

1. **Dovobet and — proprietary names provide brand recognition to healthcare providers**

*LEO Pharmaceutical Products Ltd. (LEO Pharma A/S) has consulted the in preparing this response to DMETS review comments for the DOVOBET tradename and recognize DMETS' concern related to look-alike and sound-alike confusion between Dovobet and Dovonex. LEO appreciated the recommendations received from DMETS to alter the Dovobet tradename and the packaging material in order to differentiate the two tradenames from each other. In addition, we acknowledge the FDA's recognition that there are orthographic differences between the last syllables that make these two proprietary names distinct. These include the distinct — portion of — as compared to the "nex" of Dovonex.*

*We believe that there is a significant benefit to the health care community for maintaining the brand recognition of Dovonex. Dovonex has market recognition with the active ingredient calcipotriene. Maintaining the association of " — for calcipotriene and introducing the ' — for betamethasone, will assist patients, physicians, pharmacists, and nurses to know the active ingredients of the product. We believe that introducing a unique and different proprietary name introduces the risk that patients who currently use Dovonex might use the combination product without knowing the difference. However, this branding strategy has been safely used by many pharmaceutical companies in naming combination drug products. Some examples include:*

- |                           |     |                                                |
|---------------------------|-----|------------------------------------------------|
| • Darvon (Propoxyphene)   | vs. | Darvocet (Propoxyphene and Acetaminophen)      |
| • Lotrimin (Clotrimazole) | vs. | Lotrisone (Clotrimazole and Betamethasone)     |
| • Cozaar (Losartan)       | vs. | Hyzaar (Losartan and Hydrochlorothiazide)      |
| • Inderal (Propranolol)   | vs. | Inderide (Propranolol and Hydrochlorothiazide) |
| • Tenormin (Atenolol)     | vs. | Tenoretic (Atenolol and Chlorthalidone)        |
| • Capoten (Captopril)     | vs. | Capozide (Captopril and Hydrochlorothiazide)   |

**DMETS Response:**

DMETS acknowledges that the proprietary names — and Dovonex may provide brand recognition to healthcare providers. However, we remain concerned with the look-alike and sound-alike similarities between the two names for safety reasons. As we stated previously, prescriptions for either product may be written with "as directed" directions for use. Thus, brand recognition will not be helpful at the time when the practitioner interprets the prescription. The pharmacist or dispensing professional may misinterpret the names regardless of brand recognition. Upon launch of the new product, brand recognition of Dovonex may lead to medication errors until practitioners become familiar with the new product, — The additional product characteristic similarities including dosage form (ointment) and dispensing quantity (30 g 60 g, and — es), if included on a prescription, may increase the potential for confusion. Moreover, DMETS has postmarketing evidence of name confusion reported with some of the name pairs the Sponsor has cited as examples of existing product names with brand recognition. DMETS notes that all of the name pairs stated have been available on the U.S. market for over 10 years, prior to the existence of DMETS, and the Agency's methodology and review for potential name confusion.

2. **lettering will differentiate the name from Dovonex**

Furthermore, LEO suggests utilizing " " letters as a risk management tool to highlight the different portion of the two names. This technique has been used to differentiate approved proprietary and non-proprietary names by the FDA. An example includes when medication errors were reported with Lamisil. We proposed the appearance as: , which will appear on the labels and labeling of the product. LEO believed that this along with the other actions taken, as described below, will indeed differentiate the name from Dovonex and therefore kindly request the Agency to reconsider its recommendation not to use the proprietary name .

**DMETS Response:**

DMETS acknowledges that " " lettering is useful, when used appropriately, to decrease the potential of product selection error. However, the technique has been employed postmarketing to help distinguish products with known confusion. In this case, we recognize the confusion before marketing and thus believe the name should be revised prior to error. Additionally, most prescribers do not use " " lettering when they write a proprietary name on a prescription. If a prescriber writes a prescription for without the " " lettering (i.e., ), the potential for misinterpretation remains high due to the look-alike similarities between and Dovonex. Thus, although DMETS acknowledges that " " lettering may help differentiate between the packaging and labeling for the two names thereby decreasing the potential for product selection error, it will not likely decrease the potential for misinterpretation of a written prescription by the pharmacist or dispensing practitioner.

3. **Risk of steroid-related effects is very small if was accidentally used instead of Dovonex for a limited treatment period.**

Physicians, pharmacists, and patients are in our opinion able to recognize and distinguish the two products from each other. Both active substances are used for treatment of psoriasis in sequential therapy. Typically, for initial or acute treatment of psoriasis plaques, J or a steroid alone is used followed by Dovonex. For treatment outcome or safety reasons, both products can be used at any phase of psoriasis treatment. The products may be used in an alternating fashion in pulse therapy. Treatment efficacy and safety have been shown in several studies for both products alone and also for sequential or pulse combination regimes of both products.

Both products are effective and safe treatments for patients with psoriasis vulgaris amenable to topical treatment. " " reduces symptoms faster than Dovonex and therefore presents a convenience benefit during acute disease phases. However, the patient's condition is not expected to fail to improve or worsen if Dovonex is used instead of " "

The safety profile of " " is based upon data from more than 3000 patients treated with " " ointment. Regarding risk of local adverse effects, skin atrophy was infrequent (0.1%) and hypopigmentation reported in less than 1% (NDA 21-852, Module 2, Clinical Overview; 2.5.5.14). These effects are known to be associated mainly with prolonged use of potent topical steroids and " " intment has been shown to be safe also when used as required for up to 52 weeks (NDA 21-852, Module 2, Clinical Overview; 2.5.5.9). Systemic effects have been investigated in terms of HPA axis

suppression and no cases were reported for [redacted] ointment, even in patients with very extensive psoriasis (NDA 21-852, Module 2, Clinical Overview; 2.5.3.1). Thus, the risk of steroid-related effects if [redacted] was accidentally used instead of Dovonex for a limited treatment period is very small.

**DMETS Response:**

DMETS acknowledges that both Dovonex and [redacted] are used for treatment of psoriasis in sequential therapy. However, we cannot state with assurance that there is very small risk to the patient should they receive the wrong product. It is the prescribing practitioner's decision as to which therapy is most appropriate at what stage of the disease process. Regardless of the safety profile of either product, should the patient receive the wrong product, it will not be the product the prescriber intended to use. Thus, any confusion is not considered acceptable even if the risk of adverse events is very small.

**4. Different product characteristics and different packaging for [redacted] ointment and Dovonex ointment will help differentiate the products from each other.**

*The outer packaging of [redacted] ointment differs significantly from the outer packaging of Dovonex ointment which helps distinguish the two products from each other. As shown below, the Dovonex ointment carton is presented in the colors of green/turquoise and white, whereas the proposed carton package for [redacted] ointment is a neutral white package with black text and red stripes. Even if the two products are located next to each other on pharmacy shelves, the design of the packaging material will help differentiate the products from each other, thus minimizing the potential user error. (graphics of both packages)*

*DMETS states that many overlapping product characteristics between Dovonex and [redacted] may increase the potential for confusion; however, LEO finds that many of these product characteristics may be of benefit for both the prescriber and patients. The fact that the prescriber and patient population is identical for the two products may be beneficial as doctors and patients are well introduced to "Dovo"nex, which in the U.S. is well-known, established, and perceived as calcipotriene, an effective treatment of psoriasis vulgaris. Doctors are- and patients eventually will be able to recognize and separate the two products from each other. The [redacted] name emphasizes with its last syllable "bet" the other active compound betamethasone dipropionate, which is also used for the treatment of psoriasis and has been available on the U.S. market in several topical formulations (such as Alphatrex, and Betamethasone dipropionate from various manufacturers.) This intuitive perception of two active compounds associated with the product name [redacted] supports patient and doctors in the distinction of the two products. Furthermore, and because of the steroid compound which is associated with the name, efficacy expectations from doctors and patients toward the two products is different. This is, at least, our experience from other countries in Europe where both names co-exist with each other. This has also been confirmed in market analyses performed to monitor the immediate association of doctors to the name Dovobet/Daivobet in countries where Dovonex/[redacted] and Daivonex/[redacted] co-exist (see appendix I and II for lists of countries where the two names co-exist.)*

*The strength of the active ingredient, calcipotriol, is identical in the two products; however [redacted] also contains the active ingredient, betamethasone, which clearly*

*distinguishes the two products. The names of the active ingredients will also be printed on the packaging materials of Dovonex ointment and \_\_\_\_\_ ointment.*

*Indication for use, route of administration, and dosage formulation are similar for both products, Dovonex ointment and \_\_\_\_\_ ointment, however this again may eventually ensure correct use of both products used by the same patient for this same disease.*

**DMETS Response:**

DMETS acknowledges that the carton labeling and container labels for Dovonex (green/turquoise package with white text) and \_\_\_\_\_ (neutral white package with black text and red stripes) have distinctly different colors which may help differentiate between the two products. Additionally, the tall man lettering on the \_\_\_\_\_ packaging may help decrease the potential for the wrong product being selected should the two products be located together on pharmacy shelves.

However, DMETS remains concerned about the overlapping product characteristics between Dovonex and \_\_\_\_\_, as we stated in our response in section 1 above. The Sponsor has discussed the importance of brand recognition with Dovonex and \_\_\_\_\_ for the prescribers and patients, but has not addressed another important link in the chain, the potential for confusion during interpretation of the prescription by a pharmacist or dispensing professional. The two names have look and sound-alike similarities, in addition to shared product characteristics, such as the ointment dosage form and overlapping dispensing quantities (30 g, 60 g, and \_\_\_\_\_ tubes). Brand recognition by the prescriber and patients will have no impact on how a pharmacist interprets a written or verbal prescription at the time of dispensing. In fact, upon launch of the new product, brand recognition of Dovonex may lead to medication errors because practitioners won't be familiar with the new product and may think the prescriber meant to order Dovonex.

DMETS acknowledges the Sponsor's list in Appendix 1 of the countries in which Dovonex/ \_\_\_\_\_ ointment and Daivonex/ \_\_\_\_\_ ointment are approved and marketed. However, to DMETS knowledge, none of the countries that are cited have a formal medication error reporting program. Thus, the claims that those markets have not experienced any mix-ups between the tradenames, or that the countries have not received any medication errors reports can be misleading. DMETS maintains that if there is no medication error reporting program, it is possible that such errors have occurred, but would not be reported.

**5. Incorporation of most of DMETS suggestions to the container labels and carton in order to differentiate the packaging material.**

*LEO has taken these comments into consideration and has followed most of DMETS suggestions to alter the container labels and carton in order to differentiate the packaging material for the two products further. Please see our separate response submitted on September 16, 2005 and the proposed outer packaging for \_\_\_\_\_ ointment above. Furthermore, LEO has added a barcode to the proposed carton for \_\_\_\_\_ ointment which we believe will help minimize medication/dispensing errors.*

from the searches. In addition, for each name 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.

1. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary names,            / Taclonex. 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.

- a. DDMAC finds the proprietary names,            / taclonex, acceptable from a promotional perspective.
- b. The Expert Panel identified three proprietary names that were thought to have the potential for confusion with I            . These products are listed in Table 1 (see page 9), along with the dosage forms available and usual dosage.
- c. The Expert Panel identified three proprietary names that were thought to have the potential for confusion with Taclonex. These products are listed in Table 2 (see page 9), along with the dosage forms available and usual dosage

Table 1: Potential Sound-Alike/Look-Alike Names Identified for \_\_\_\_\_

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
_____	Calcipotriene 0.005% and Betamethasone _____ Ointment: 15 g, 30 g, 60 g, _____ tubes	Apply an adequate layer of ointment to the affected area once daily and rub in gently and completely.	N/A
<b>Darvocet A500</b> <b>Darvocet N-100</b> <b>Darvocet N-50</b>	<b>Propoxyphene/Acetaminophen</b> Tablets: 100 mg/500 mg Tablets: 100 mg/650 mg Tablets: 50 mg/325 mg	Darvocet N-100 and Darvocet A500: 1 tablet PO every 4—6 hours as needed for pain. Maximum dose should not exceed propoxyphene napsylate 600 mg/day and acetaminophen 4000 mg/day. Darvocet N-50: 1—2 tablets PO every 4 hours as needed for pain. Maximum dose should not exceed propoxyphene napsylate 600 mg/day and acetaminophen 4000 mg/day (12 tablets).	SA/LA
<b>Dermabet</b>	Betamethasone Valerate eq 0.1% base Cream: 15 g and 45 g tubes	Apply to affected areas one to three times a day. Dosage once or twice a day is often effective. Occlusive dressings may be used for psoriasis.	LA/SA
<b>Dovonex</b>	Calcipotriene 0.005% Ointment: 30 g, 60 g, 100 g, 120 g tubes Cream: 30 g, 60 g, 100 g, 120 g tubes Solution: 60 mL bottles	Apply twice daily	LA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

Table 2: Potential Sound-Alike/Look-Alike Names Identified for Taclonex

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
<b>Taclonex</b>	Calcipotriene 0.005% and Betamethasone _____ Ointment: 15 g, 30 g, 60 g, _____ tubes	Apply an adequate layer of ointment to the affected area once daily and rub in gently and completely.	N/A
<b>Lotronex</b>	Alosetron Tablets: 0.5 mg, 1 mg	Marketed with restrictions and mandatory physician enrollment.  <u>Adult females &gt;= 18 years:</u> Initially, 1 mg PO once daily for 4 weeks. After 4 weeks, if IBS symptoms are not adequately controlled but the drug is well tolerated, the dose may be increased to 1 mg PO twice per day for 4 weeks. Discontinue the drug in those patients whose symptoms are not adequately controlled after 4 weeks of treatment with 1 mg PO twice per day.	LA
<b>Faslodex</b>	Fulvestrant Solution for Injection: 50 mg/mL	<u>Adult females, including the elderly:</u> 250 mg via intramuscular injection, once monthly as either a 5 ml injection or 2 concurrent 2.5 ml injections	LA
<b>Lactinex (OTC)</b>	Lactobacillus Acidophilus, Lactobacillus Bulgaricus Chewable Tablets: "mixed culture" (no dosage unit)	<u>Adults and children:</u> 4 chewable tablets by mouth 3—4 times per day.	LA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

2. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

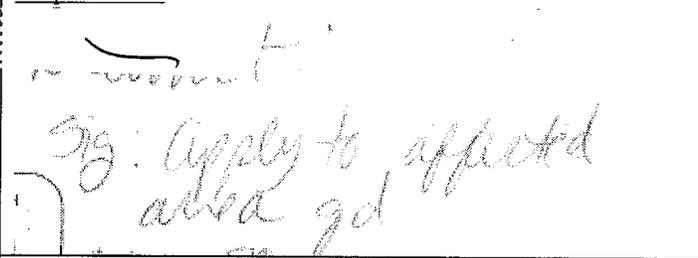
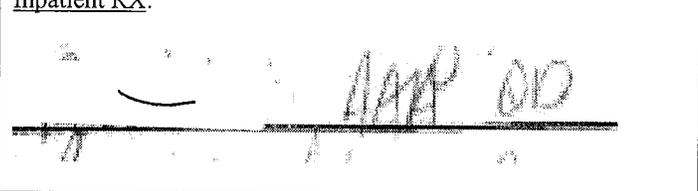
As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to            Taclonex were discussed by the Expert Panel (EPD).

3. PRESCRIPTION ANALYSIS STUDIES

Methodology:

Three separate studies were conducted within the Centers of the FDA for each proposed proprietary name to determine the degree of confusion of            Taclonex 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. Each set of 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            Taclonex (see pages 10-11). 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.

a.           

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> 	<p><u>          </u> at, 80 grams. Apply to affected area once a day"</p>
<p><u>Inpatient RX:</u></p> 	

b. Results for —

There was confirmation that — could be confused with Darvocet. One respondent from the outpatient written study and one respondent from the inpatient written study misinterpreted the proposed name as Darvocet (n=2), an already existing marketed drug product. Additionally, one respondent from the outpatient written study interpreted — as “Daivoliet, comment: looks a lot like Darvocet, although this is topically applied and that is orally ingested.” Furthermore, another respondent from the outpatient written study interpreted — correctly but commented “this looks like Darvocet when written. However, the cream part is distinguishing.” 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. See Appendix A (page 32) for the complete listing of interpretations from the verbal and written studies.

c. Taclonex

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> <p>Taclonex            apply to affected area once            daily 30g tube</p>	<p>“Taclonex, please dispense a 30 gram tube. Apply to affected area once a day”</p>
<p><u>Inpatient RX:</u></p> <p><del>Taclonex apply to affected area qd</del></p>	

d. Results for Taclonex:

None of the interpretations of the proposed name, Taclonex, overlap, sound similar, or look similar to any currently marketed U.S. product. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Taclonex. 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 small sample size. See Appendix B (page 33) for the complete listing of interpretations from the verbal and written studies.

#### 4. INDEPENDENT NAME ANALYSIS

The \_\_\_\_\_ conducted a research study and risk assessment to evaluate the potential for error between \_\_\_\_\_ and currently marketed proprietary or non-proprietary names of drugs in the United States. The \_\_\_\_\_ reported that 106 physicians, 102 pharmacists, and 42 nurses participated in the study sections. The specialties of the physicians and pharmacists, when specified, were: dermatologists (78), general practitioners/family practitioners/internists (28), hospital pharmacists (50), and retail pharmacists (50). These medical professionals participated in Sections II and III of the \_\_\_\_\_ study. The six sections of the study as well as the study findings are discussed below.

##### a. Section I – Internal Expert Panel Discussion

The staff at \_\_\_\_\_ conducted searches of “standard published drug references” in order to identify sound-alike or look-alike proprietary and nonproprietary names marketed in the U.S. References were also used to identify medical terms, acronyms, and/or abbreviations that could potentially conflict with \_\_\_\_\_. The panel was convened to identify potential safety concerns between the test name and marketed product names.

The panel members identified the following names as being potentially similar to \_\_\_\_\_: Darvocet-N, DDAVP, Dermabet, Diabeta, Dovonex, Temovate, and Ultravate. No medical terms were regarded as “an apparent issue for the prescribing and dispensing of \_\_\_\_\_”. No acronyms/abbreviations related to the prefix/suffix of \_\_\_\_\_ were identified that were regarded as apparent issues for the prescribing/dispensing of \_\_\_\_\_.

##### ***DMETS Response:***

DMETS also identified Darvocet, Dermabet, and Dovonex as names which could be confused orthographically and phonetically with \_\_\_\_\_. DMETS disagrees with \_\_\_\_\_ conclusions regarding Dermabet. Dermabet and Dovonex are discussed further in this review (see pages 17-18). The potential for confusion between \_\_\_\_\_ and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with \_\_\_\_\_ due to a lack of convincing look-alike/sound-alike similarities with \_\_\_\_\_ in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, or dosage formulation.

##### b. Section II – Rx Studies – Prescription Collection

Ten health care professionals (six physicians, two pharmacists, and two nurses) produced verbal and handwritten prescriptions for \_\_\_\_\_. \_\_\_\_\_ included prescriptions of currently marketed drug names in the prescription studies to provide for a control. Each health care professional provided one verbal and two handwritten (inpatient and outpatient) prescriptions for every test name, including \_\_\_\_\_.

c. Section III - Rx Studies – Interpretation and Safety Surveys

elicited 240 U.S. health care professionals to interpret the prescriptions. Eighty health care professionals were assigned to each group (Verbal, Handwritten - Inpatient, or Handwritten - Outpatient). Once the health care professionals have interpreted the prescriptions, they complete self-administered questionnaires. The health care professionals were asked to identify proprietary or nonproprietary drug names that may sound like and/or look like the proposed proprietary name.

In the verbal prescription study (n=80), was not misinterpreted for any existing brand/generic drug name. In the handwritten inpatient prescription study (n=80), 72 of 80 health care professionals did not misinterpret for any existing brand/generic name. The remaining eight professionals misinterpreted the name as Darvocet. In the handwritten outpatient prescription study (n=80), 77 of 80 health care professionals did not misinterpret for any existing brand/generic name. The remaining three professionals misinterpreted the name as Darvocet. stated that “concern is decreased because Darvocet shares no commonalities with the test product. Additionally, Darvocet is no longer marketed, and no therapeutic equivalents are available.” Additionally, nine names were identified as having similar sound and/or look-alike similarities with and were further evaluated by . These nine names were Aldomet, Caduet, Darvocet, Darvon, Daypro, Diabeta, Diovan, Dolobid, and Dovonex. concluded that when compared to , minimal overlapping drug product characteristics were identified that would contribute to a medication error.

***DMETS Response:***

DMETS also identified Darvocet, Dermabet, and Dovonex as names which could be confused orthographically and phonetically with . DMETS disagrees with conclusions regarding Dermabet and Dovonex. Dermabet and Dovonex are discussed further in this review (see pages 17-18). The proprietary name “Darvocet” (which lacks a modifier) is no longer marketed, however, the Darvocet product line is comprised of Darvocet-N 50 (50 mg/325 mg), Darvocet A500 (100 mg/500 mg), and Darvocet-N 100 (100 mg/650 mg), which are still marketed. The potential for confusion between and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with due to a lack of convincing look-alike/sound-alike similarities with , in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage formulation.

d. Section IV – Computerized Orthographic and Phonologic Analysis (COPA)

conducted a computerized orthographic and phonologic analysis to evaluate the degree of look-alike (orthographic) and sound-alike (phonologic) similarity for all drug names identified in the research relative to , including drug names originating from all sections of the study.

The names Darvocet, Darvocet-N, Darvon, Darvon-N, and Diabeta were found to exceed overall similarity threshold values in the COPA results. [redacted] luded that when compared to [redacted], minimal overlapping drug product characteristics were identified that would contribute to a medication error.

**DMETS Response:**

DMETS also identified Darvocet as a name which could be confused orthographically and phonetically with [redacted]. The potential for confusion between [redacted] and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with [redacted] in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage formulation.

DMETS notes that in addition to the names stated above (Darvocet, Darvocet-N, Darvon, Darvon-N, and Diabeta) as exceeding the overall similarity threshold values, the names Dermabet and Dovonex also exceeded the threshold values in the orthographic results. Dermabet and Dovonex have similar product characteristics with [redacted] and thus we think the potential for confusion is increased.

e. Section V – [redacted] ference Comparative Safety Analysis

The [redacted] ference Comparative Safety Analysis provided a side-by-side comparison of the test product's attributes versus those of the marketed products that were identified as being potentially similar by the [redacted] rnal Expert Panel Discussion, healthcare professional survey inputs, prescription studies, and COPA (Study Sections I through IV).

Results of [redacted] ference Comparative Safety Analysis identified four products, Del-Beta, Dermabet, Dovonex, and Ultravate, which shared three or more commonalities with [redacted]

**DMETS Response:**

DMETS acknowledges the [redacted] mparative Safety Analysis and considers two of the names (Del-Beta and Ultravate) to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with [redacted] in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage formulation. However, DMETS does not agree with the conclusions of the study regarding the proprietary names Dermabet and Dovonex. Dermabet and Dovonex are discussed on pages 17-18 of this review.

f. Section VI – External Advisory Committee (EAC)

Eight health care practitioners on the External Advisory Committee with experience in adverse events, patient safety, and/or risk management reviewed the proposed proprietary name, [redacted] and identified any potential sound-alike and/or look-alike names of marketed drug products.

The External Advisory Committee identified three names, Diovan, Darvocet, and Diabeta, as having similar sound and/or appearance to [redacted]. The EAC concluded that when compared to [redacted] minimal overlapping drug product characteristics were identified that would contribute to a medication error. The EAC found the proposed proprietary name to be an acceptable candidate for the proposed product.

***DMETS Response:***

DMETS also identified Darvocet as a name which could be confused orthographically with [redacted]. The potential for confusion between [redacted] and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with Daivobet, in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage formulation.

The [redacted] concluded that “The results of the [redacted] search favorably supports the use of [redacted] as a proposed proprietary name for LEO Pharm’s proposed product for psoriasis vulgaris.”

***Conclusion:***

DMETS does not agree with the overall conclusions of the “Proprietary Name Safety Assessment” regarding the proprietary name [redacted]. We remain concerned with the look-alike/sound-alike similarities with Dermabet, in addition to the overlapping product characteristics which include; active ingredient (betamethasone), indication for use (psoriasis), frequency of administration (once daily), and route of administration (topical). Additionally, we remain concerned with the look-alike similarities with Dovonex, in addition to the overlapping product characteristics which include; active ingredient (calcipotriene), prescriber population (dermatologists), ordered quantity (30 grams, 60 grams, and 100 grams), treatment duration (chronic), product strength (0.005%), indications for use (psoriasis), route of administration (topical), dosage formulation (ointment), and patient population (psoriasis patients).

5. SAFETY EVALUATOR RISK ASSESSMENT

a. [redacted] Name Review

In reviewing the proprietary name, J [redacted] the primary concerns related to look-alike and sound-alike confusion with Darvocet, Dovonex, and Dermabet.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that \_\_\_\_\_ could be confused with Darvocet. One respondent from the outpatient written study and one respondent from the inpatient written study misinterpreted the proposed name as Darvocet (n=2), an already existing marketed drug product. Additionally, one respondent from the outpatient written study interpreted \_\_\_\_\_ as "Daivoliet, comment: looks a lot like Darvocet, although this is topically applied and that is orally ingested." Furthermore, another respondent from the outpatient written study interpreted \_\_\_\_\_ correctly but commented "this looks like Darvocet when written. However, the cream part is distinguishing". 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.

- i. \_\_\_\_\_ may look similar to Dermabet when scripted. Dermabet is a currently marketed prescription topical steroid cream containing Betamethasone Valerate, one of the two drugs also contained in \_\_\_\_\_. Dermabet is used to treat topical steroid responsive dermatoses, including psoriasis. Dermabet is applied one to three times a day to the affected area. The two names have orthographic similarities including the same word length (8 letters), the same beginning letter \_\_\_\_\_ and the same prefix \_\_\_\_\_. The middle portion of the name '\_\_\_\_\_n' \_\_\_\_\_ may also look like the middle portion of the name '-erma-' in Dermabet, especially if the dot in the letter \_\_\_\_\_ is left off or lacks prominence, or if the name is not scripted clearly (see below). Additionally, both Dermabet and \_\_\_\_\_ are available in only one strength and one dosage formulation, thus it is possible that the product strength and formulation will be omitted on an order and a product will still be dispensed. Furthermore, topical products are often prescribed with "as directed" directions for use. Thus, lack of a differentiating product strength, dosage formulation, or directions for use included on a prescription order may not help to differentiate between the two names. Furthermore, the two names Dermabet and \_\_\_\_\_ have multiple overlapping product characteristics such as; active ingredient (betamethasone), indication for use (psoriasis), frequency of administration (once daily), route of administration (topical), prescriber population (dermatologists), ordered quantity (15 grams), and treatment duration (chronic). Therefore, due to strong orthographic similarities, as well as numerous overlapping product characteristics, DMETS does not believe that these two products should co-exist in the marketplace due to the potential for confusion.

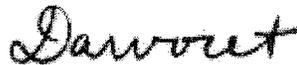
- ii.            can look similar to Dovonex when scripted. Dovonex is indicated for the treatment of moderate plaque psoriasis and is available in 0.005% ointment, 0.005% cream, and 0.005% solution. Dovonex is applied to affected area(s) twice daily. Dovonex contains Calcipotriene as the single active ingredient while            contains Calcipotriene in combination with the corticosteroid Betamethasone. The similar beginning letters shared between Dovonex and            is           .            is the principal contribution to the look-alike similarities of the two names. Furthermore, the letter “x” in Dovonex can look similar to the letter “x” in           , depending on how it is scripted (see sample below).

However,            contains the upstroke letter “x”, which, if scripted prominently, may help differentiate the names orthographically. Dovonex is supplied in multiple dosage forms (ointment, cream, and solution). Thus, the intended dosage form will either be stated on the order or obtained from the prescriber prior to dispensing. This dosage form designation will help to differentiate the two names on a prescription and help to minimize the potential for medication errors. However, both products are available as ointments and thus, inclusion of this dosage form on an order may not help to minimize the confusion between the name pair. While the frequency of application (twice daily vs. once daily) is another product characteristic that may help to distinguish Dovonex from           , it is not unlikely to have topical products ordered with “as directed” directions for use. Therefore, even though Dovonex and            have different dosing frequencies, this product characteristic may not help distinguish between the two names on an order that is written with “as directed” directions for use. Thus, a prescription written for “Dovonex Oint., 30 grams or 1 tube, apply as directed” may be misinterpreted as “           Oint., 30 grams or 1 tube, apply as directed” and vice versa. If            is inadvertently dispensed instead of Dovonex, the patient would be exposed a high potency corticosteroid (i.e., betamethasone dipropionate) and may experience the local (e.g., atrophy and hypopigmentation) and systemic (e.g., hypothalamic-pituitary-adrenal axis (HPA) suppression) adverse effects associated with topical corticosteroids. If Dovonex is inadvertently dispensed instead of           , the patient will not receive the benefits of the corticosteroid the prescriber intended the treatment to include and thus, the patient’s condition may fail to improve or worsen. Furthermore, whether the drugs are stored by proprietary name or by route of administration (topical), they will likely be stored next to each other on pharmacy shelves. This may lead to selection errors among these products due to their similar names. Moreover, Dovonex and            have many overlapping product characteristics including prescriber population (dermatologists), ordered quantity (30 grams, 60 grams, and 100 grams), treatment duration

(chronic), product strength (0.005%), indication for use (psoriasis), route of administration (topical), dosage formulation (ointment), and patient population (patients with psoriasis). The orthographic similarities, overlapping product characteristics, and potential for similar prescribing directions (use as directed), increase the potential for confusion involving this name pair. Thus, DMETS does not believe that these two products should co-exist in the marketplace due to the potential for confusion.

- iii. — was identified to have look and sound-alike similarities to the proprietary name, Darvocet. Darvocet, a combination product composed of acetaminophen and propoxyphene, is indicated for the relief of mild to moderate pain. The proprietary name “Darvocet” (which lacks a modifier) is no longer marketed, however, the Darvocet product line is comprised of Darvocet-N 50 (50 mg/325 mg), Darvocet A500 (100 mg/500 mg), and Darvocet-N 100 (100 mg/650 mg), which are still marketed. The usual adult dose is one to two tablets every four hours as needed. Orthographic similarities may be attributed to endings, “ — ’ vs. “ — ”, which can look alike when scripted in cursive (see sample below).



Additionally, both names — with the letter ‘ — and the letter — in Darvocet can look like the letters — n — . However, the upstroke characteristic of the letter ‘ — i r — may help the names look different if scripted prominently. Since Darvocet is available in multiple strengths, the strength of Darvocet must be indicated by use of the modifier or by writing out the strength (e.g., Darvocet-N 100 or Darvocet 100 mg/650 mg). The necessary inclusion of the modifier or strength will help to differentiate Darvocet from ‘ — , a prescription order. Furthermore, the dose written for Darvocet will likely include at least one numeral (e.g., 1 to 2 tablets every four hours) or a dispensing quantity while the dose for ‘ — will not usually contain any numerals (e.g., apply to affected area twice daily). It is possible for an order to be written for “ — Xd” however this is not common and the presence of numerals in the dose on an order for Darvocet may help distinguish these products from one another. Despite orthographic similarities, DMETS believes the likelihood for confusion between Darvocet and — minimal due to the aforementioned reasons.

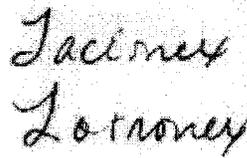
b. Taclonex Name Review

In reviewing the proprietary name, Taclonex, the primary concerns related to look-alike and sound-alike confusion with Lotronex, Lactinex, and Faslodex.

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. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Taclonex. 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 small sample size.

- i. Lotronex was identified to have look-alike similarities to the proposed name, Taclonex. Lotronex is an oral, selective serotonin 5-HT<sub>3</sub> receptor antagonist. It is approved with restrictions for the treatment of women who exhibit severe diarrhea-predominant irritable bowel syndrome (IBS) and have failed conventional therapy. The dose of Lotronex is 1 mg by mouth once or twice daily. The two names share orthographic similarities due to the shared suffix, '-onex'. Additionally, the letter 'T' in Taclonex can resemble a capitalized letter 'L' when scripted in cursive (see example below).

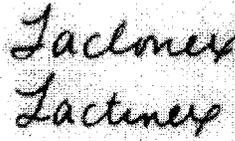


The image shows two lines of handwritten text in cursive. The top line reads 'Taclonex' and the bottom line reads 'Lotronex'. The letters 'T' and 'L' are written in a way that they are very similar in shape, illustrating the potential for confusion mentioned in the text.

Furthermore, each name contains an upstroke in similar positions of the name due to the letter 'l' in Taclonex and the letter 't' in Lotronex. If the letter t is not crossed the upstrokes may look identical. However, Taclonex contains the letters 'a' and 'c' between the two upstrokes whereas Lotronex contains the single letter 'o' which may help differentiate between the two names. Furthermore, Lotronex is marketed with restrictions under a risk management program with mandatory physician and patient enrollment in the program. Thus, Lotronex will be prescribed by specialists for a specific patient population which is educated about Lotronex which will therefore decrease the potential for confusion with Taclonex. Moreover, there are numerous product differences between Lotronex and Taclonex, such as: indication of use (psoriasis vs. IBS), dosage form (ointment vs. tablet), product strength (0.05%/0005% vs. 0.5 mg or 1 mg), and route of administration (topical vs. oral). DMETS believes the likelihood for confusion between Taclonex and Lotronex is minimal due to the aforementioned reasons.

- ii. Lactinex was identified to have look-alike similarities to the proposed name, Taclonex. Lactinex is an over-the-counter (OTC) nutritional supplement which contains active mixed cultures of *Lactobacillus acidophilus* and *Lactobacillus Bulgaricus*. Lactinex is taken as four tablets orally three to four times daily. Lactobacillus species are acid-producing probiotic bacterium that are often taken to help relieve diarrhea. Lactinex and Taclonex share the same suffix ending '-nex' which

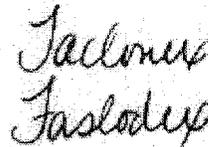
contributes to the orthographic similarities. Additionally, the letter 'T' in Taclonex can resemble a capitalized letter 'L' when scripted in cursive (see example below).



The image shows two lines of handwritten cursive text. The first line reads 'Taclonex' and the second line reads 'Lactinex'. The letters 'T' in 'Taclonex' and 'L' in 'Lactinex' are written in a similar cursive style, illustrating how they can be confused when written quickly.

Furthermore, each name contains an upstroke in similar positions of the name due to the letter 'l' in Taclonex and the letter 't' in Lactinex. If the letter 't' in Lactinex is not crossed, the upstrokes may look identical. However, Lactinex is available OTC as a nutritional supplement, therefore it is not likely that a prescriber would write a prescription for Lactinex. Taclonex is available by prescription only, thus a prescription is required. Furthermore, there are numerous product differences between Taclonex and Lactinex such as: indication of use (psoriasis vs. diarrhea), dosage form (ointment vs. tablet), route of administration (topical vs. oral), frequency of administration (once daily vs. 3 to 4 times daily), and product classification status (prescription only vs. OTC). DMETS believes the likelihood for confusion between Taclonex and Lactinex is minimal due to the aforementioned reasons.

- iii. Faslodex was identified to have look-alike similarities to the proposed name, Taclonex. Faslodex is Fulvestrant Injection, which is the first in a new class of antiestrogens that works by degrading the estrogen receptor as opposed to blocking it. Faslodex is indicated for the treatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy. Faslodex is given as 250 mg via intramuscular injection, once monthly as either a 5 mL injection of 2 concurrent 2.5 mL injections. The two names share some look-alike similarities due to the shared suffix '-ex'. Additionally, the letter 'T' in Taclonex can resemble a capitalized letter 'F' when scripted in cursive (see example below).



The image shows two lines of handwritten cursive text. The first line reads 'Taclonex' and the second line reads 'Faslodex'. The letters 'T' in 'Taclonex' and 'F' in 'Faslodex' are written in a similar cursive style, illustrating how they can be confused when written quickly.

Furthermore, each name contains an upstroke in similar positions of the name due to the letter 'l' in Taclonex and the letter 'l' in Faslodex. However, the name Faslodex contains an additional upstroke from the letter 'd' which may help to differentiate between the two names. Taclonex is a topical product for a dermatologic indication (psoriasis), whereas Faslodex is an injectable product for administration by a health care professional as part of a chemotherapeutic regimen for metastatic breast cancer. Therefore, each product has a distinctive patient population (patients with psoriasis vs. breast cancer patients) and a distinctive

prescriber population (dermatologist vs. oncologist) which may reduce the potential for confusion. Furthermore, there are additional product differences between Taclonex and Faslodex such as: frequency of administration (once daily vs. once monthly), product strength (0.05%/0.005% vs. 50 mg/mL), and dose (adequate layer vs. 250 mg). DMETS believes the likelihood for confusion between Taclonex and Faslodex is minimal due to the aforementioned reasons.

#### IV. COMMENTS TO THE SPONSOR:

##### A. RECONSIDERATION OF DOVOBET

The sponsor has requested a re-consideration of the proprietary name, Dovobet, for Calcipotriene 0.005% and Betamethasone — Ointment. The Sponsor believes the potential for confusion between Dovobet and Dovonex is low for the following reasons (the sponsor's comments are italicized.)

##### 1. **Dovobet and — proprietary names provide brand recognition to healthcare providers**

*LEO Pharmaceutical Products Ltd. (LEO Pharma A/S) has consulted the — in preparing this response to DMETS review comments for the DOVOBET tradename and recognize DMETS' concern related to look-alike and sound-alike confusion between Dovobet and Dovonex. LEO appreciated the recommendations received from DMETS to alter the Dovobet tradename and the packaging material in order to differentiate the two tradenames from each other. In addition, we acknowledge the FDA's recognition that there are orthographic differences between the — syllables that make these two proprietary names distinct. These include the distinct ' — portion of: — as compared to the "nex" of Dovonex.*

*We believe that there is a significant benefit to the health care community for maintaining the brand recognition of Dovonex. Dovonex has market recognition with the active ingredient calcipotriene. Maintaining the association of "Dovo" for calcipotriene and introducing the — for betamethasone, will assist patients, physicians, pharmacists, and nurses to know the active ingredients of the product. We believe that introducing a unique and different proprietary name introduces the risk that patients who currently use Dovonex might use the combination product without knowing the difference. However, this branding strategy has been safely used by many pharmaceutical companies in naming combination drug products. Some examples include:*

- |                           |     |                                                |
|---------------------------|-----|------------------------------------------------|
| • Darvon (Propoxyphene)   | vs. | Darvocet (Propoxyphene and Acetaminophen)      |
| • Lotrimin (Clotrimazole) | vs. | Lotrisone (Clotrimazole and Betamethasone)     |
| • Cozaar (Losartan)       | vs. | Hyzaar (Losartan and Hydrochlorothiazide)      |
| • Inderal (Propranolol)   | vs. | Inderide (Propranolol and Hydrochlorothiazide) |
| • Tenormin (Atenolol)     | vs. | Tenoretic (Atenolol and Chlorthalidone)        |
| • Capoten (Captopril)     | vs. | Capozide (Captopril and Hydrochlorothiazide)   |

**DMETS Response:**

DMETS acknowledges that the proprietary names [redacted] and Dovonex may provide brand recognition to healthcare providers. However, we remain concerned with the look-alike and sound-alike similarities between the two names for safety reasons. As we stated previously, prescriptions for either product may be written with "as directed" directions for use. Thus, brand recognition will not be helpful at the time when the practitioner interprets the prescription. The pharmacist or dispensing professional may misinterpret the names regardless of brand recognition. Upon launch of the new product, brand recognition of Dovonex may lead to medication errors until practitioners become familiar with the new product, [redacted]. The additional product characteristic similarities including dosage form (ointment) and dispensing quantity (30 g 60 g, and [redacted] tubes), if included on a prescription, may increase the potential for confusion. Moreover, DMETS has postmarketing evidence of name confusion reported with some of the name pairs the Sponsor has cited as examples of existing product names with brand recognition. DMETS notes that all of the name pairs stated have been available on the U.S. market for over 10 years, prior to the existence of DMETS, and the Agency's methodology and review for potential name confusion.

**2. [redacted] lettering will differentiate the [redacted] name from Dovonex**

*Furthermore, LEO suggests utilizing "[redacted]" letters as a risk management tool to highlight the different portion of the two names. This technique has been used to differentiate approved proprietary and non-proprietary names by the FDA. An example includes [redacted] when medication errors were reported with Lamisil. We proposed the appearance as: [redacted] which will appear on the labels and labeling of the product. LEO believed that this along with the other actions taken, as described below, will indeed differentiate the [redacted] name from Dovonex and therefore kindly request the Agency to reconsider its recommendation not to use the proprietary name [redacted]*

**DMETS Response:**

DMETS acknowledges that "[redacted]" lettering is useful, when used appropriately, to decrease the potential of product selection error. However, the technique has been employed postmarketing to help distinguish products with known confusion. In this case, we recognize the confusion before marketing and thus believe the name should be revised prior to error. Additionally, most prescribers do not use "[redacted]" lettering when they write a proprietary name on a prescription. If a prescriber writes a prescription for [redacted] without the [redacted] lettering (i.e., [redacted]), the potential for misinterpretation remains high due to the look-alike similarities between [redacted] and Dovonex. Thus, although DMETS acknowledges that [redacted] lettering may help differentiate between the packaging and labeling for the two names thereby decreasing the potential for product selection error, it will not likely decrease the potential for misinterpretation of a written prescription by the pharmacist or dispensing practitioner.

**3. Risk of steroid-related effects is very small if [redacted] was accidentally used instead of Dovonex for a limited treatment period.**

*Physicians, pharmacists, and patients are in our opinion able to recognize and distinguish the two products from each other. Both active substances are used for treatment of psoriasis in sequential therapy. Typically, for initial or acute treatment of psoriasis plaques, [redacted] or a steroid alone is used followed by Dovonex. For*

*treatment outcome or safety reasons, both products can be used at any phase of psoriasis treatment. The products may be used in an alternating fashion in pulse therapy. Treatment efficacy and safety have been shown in several studies for both products alone and also for sequential or pulse combination regimes of both products.*

*Both products are effective and safe treatments for patients with psoriasis vulgaris amenable to topical treatment. — reduces symptoms faster than Dovonex and therefore presents a convenience benefit during acute disease phases. However, the patient's condition is not expected to fail to improve or worsen if Dovonex is used instead of —*

*The safety profile of — is based upon data from more than 3000 patients treated with — ointment. Regarding risk of local adverse effects, skin atrophy was infrequent (0.1%) and hypopigmentation reported in less than 1% (NDA 21-852, Module 2, Clinical Overview; 2.5.5.14). These effects are known to be associated mainly with prolonged use of potent topical steroids and — ointment has been shown to be safe also when used as required for up to 52 weeks (NDA 21-852, Module 2, Clinical Overview; 2.5.5.9). Systemic effects have been investigated in terms of HPA axis suppression and no cases were reported for — ointment, even in patients with very extensive psoriasis (NDA 21-852, Module 2, Clinical Overview; 2.5.3.1). Thus, the risk of steroid-related effects if — was accidentally used instead of Dovonex for a limited treatment period is very small.*

#### **DMETS Response:**

DMETS acknowledges that both Dovonex and — are used for treatment of psoriasis in sequential therapy. However, we cannot state with assurance that there is very small risk to the patient should they receive the wrong product. It is the prescribing practitioner's decision as to which therapy is most appropriate at what stage of the disease process. Regardless of the safety profile of either product, should the patient receive the wrong product, it will not be the product the prescriber intended to use. Thus, any confusion is not considered acceptable even if the risk of adverse events is very small.

#### **4. Different product characteristics and different packaging for — ointment and Dovonex ointment will help differentiate the products from each other.**

*The outer packaging of — ointment differs significantly from the outer packaging of Dovonex ointment which helps distinguish the two products from each other. As shown below, the Dovonex ointment carton is presented in the colors of green/turquoise and white, whereas the proposed carton package for — ointment is a neutral white package with black text and red stripes. Even if the two products are located next to each other on pharmacy shelves, the design of the packaging material will help differentiate the products from each other, thus minimizing the potential user error. (graphics of both packages)*

*DMETS states that many overlapping product characteristics between Dovonex and — may increase the potential for confusion; however, LEO finds that many of these product characteristics may be of benefit for both the prescriber and patients. The fact that the prescriber and patient population is identical for the two products may be beneficial as doctors and patients are well introduced to "Dovo"nex, which in the U.S. is well-known, established, and perceived as calcipotriene, an effective treatment of*

*psoriasis vulgaris. Doctors are- and patients eventually will be able to recognize and separate the two products from each other. The [redacted] name emphasizes with its last syllable "bet" the other active compound betamethasone dipropionate, which is also used for the treatment of psoriasis and has been available on the U.S. market in several topical formulations (such as Alphatrex, and Betamethasone dipropionate from various manufacturers.) This intuitive perception of two active compounds associated with the product name [redacted] supports patient and doctors in the distinction of the two products. Furthermore, and because of the steroid compound which is associated with the name, efficacy expectations from doctors and patients toward the two products is different. This is, at least, our experience from other countries in Europe where both names co-exist with each other. This has also been confirmed in market analyses performed to monitor the immediate association of doctors to the name Dovobet [redacted] in countries where Dovonex/Dovobet and [redacted] co-exist (see appendix I and II for lists of countries where the two names co-exist.)*

*The strength of the active ingredient, calcipotriol, is identical in the two products; however [redacted] also contains the active ingredient, betamethasone, which clearly distinguishes the two products. The names of the active ingredients will also be printed on the packaging materials of Dovonex ointment and [redacted] ointment.*

*Indication for use, route of administration, and dosage formulation are similar for both products, Dovonex ointment and [redacted] ointment, however this again may eventually ensure correct use of both products used by the same patient for this same disease.*

#### **DMETS Response:**

DMETS acknowledges that the carton labeling and container labels for Dovonex (green/turquoise package with white text) and [redacted] (neutral white package with black text and red stripes) have distinctly different colors which may help differentiate between the two products. Additionally, the tall man lettering on the [redacted] packaging may help decrease the potential for the wrong product being selected should the two products be located together on pharmacy shelves.

However, DMETS remains concerned about the overlapping product characteristics between Dovonex and [redacted], as we stated in our response in section 1 above. The Sponsor has discussed the importance of brand recognition with Dovonex and [redacted] for the prescribers and patients, but has not addressed another important link in the chain, the potential for confusion during interpretation of the prescription by a pharmacist or dispensing professional. The two names have look and sound-alike similarities, in addition to shared product characteristics, such as the ointment dosage form and overlapping dispensing quantities (30 g, 60 g, and [redacted] tubes). Brand recognition by the prescriber and patients will have no impact on how a pharmacist interprets a written or verbal prescription at the time of dispensing. In fact, upon launch of the new product, brand recognition of Dovonex may lead to medication errors because practitioners won't be familiar with the new product and may think the prescriber meant to order Dovonex.

DMETS acknowledges the Sponsor's list in Appendix 1 of the countries in which Dovonex/Dovobet ointment and [redacted] ointment are approved and marketed. However, to DMETS knowledge, none of the countries that are cited have a formal medication error reporting program. Thus, the claims that those markets have not experienced any mix-ups between the tradenames, or that the countries have not received any medication errors reports can

be misleading. DMETS maintains that if there is no medication error reporting program, it is possible that such errors have occurred, but would not be reported.

**5. Incorporation of most of DMETS suggestions to the container labels and carton in order to differentiate the packaging material.**

*LEO has taken these comments into consideration and has followed most of DMETS suggestions to alter the container labels and carton in order to differentiate the packaging material for the two products further. Please see our separate response submitted on September 16, 2005 and the proposed outer packaging for \_\_\_\_\_ ointment above. Furthermore, LEO has added a barcode to the proposed carton for \_\_\_\_\_ ointment which we believe will help minimize medication/dispensing errors.*

**DMETS Response:**

DMETS has re-reviewed the container labels, carton and insert labeling from a safety perspective. We note that the Sponsor has adequately addressed most of our recommendations from the original consult (ODS Consult 05-0123). However, DMETS has still identified the following areas of possible improvement, which might minimize potential user error.

a. CONTAINER LABEL (15 g, 30 g, 60 g and \_\_\_\_\_)

We have no additional comments.

b. CARTON LABELING (15 g, 30 g, 60 g and \_\_\_\_\_)

We have no additional comments.

c. INSERT LABELING

DOSAGE AND ADMINISTRATION Section

The statement "Dovobet ointment should....." has been revised to read "Apply an adequate layer of Dovobet ointment to the affected area once daily and rub in gently and completely." Use of the quantifier "adequate" may be confusing to patients and lead them to apply more product than necessary. What is an "adequate" amount of ointment? Please provide more detail in this section.

d. PATIENT INSERT LABELING

We recommend that you submit the patient insert labeling to the Division of Surveillance, Research, and Communication Support (DSRCS) for review and comment.

In summary, the Sponsor has not submitted persuasive evidence to diminish our concerns with potential confusion between Dovonex and \_\_\_\_\_

**B. INDEPENDENT NAME REVIEW OF \_\_\_\_\_**

The \_\_\_\_\_ conducted a research study and risk assessment to evaluate the potential for error between \_\_\_\_\_ and currently marketed \_\_\_\_\_

proprietary or non-proprietary names of drugs in the United States. They reported that 106 physicians, 102 pharmacists, and 42 nurses participated in the study sections. The specialties of the physicians and pharmacists, when specified, were: dermatologists (78), general practitioners/family practitioners/internists (28), hospital pharmacists (50), and retail pharmacists (50). These medical professionals participated in Sections II and III of the study. The six sections of the study as well as the study findings are discussed below.

#### 1. Section I – Internal Expert Panel Discussion

The staff at [redacted] conducted searches of “standard published drug references” in order to identify sound-alike or look-alike proprietary and nonproprietary names marketed in the U.S. References were also used to identify medical terms, acronyms, and/or abbreviations that could potentially conflict with [redacted]. A panel was convened to identify potential safety concerns between the test name and marketed product names.

The panel members identified the following names as being potentially similar to [redacted] Darvocet-N, DDAVP, Dermabet, Diabeta, Dovonex, Temovate, and Ultravate. No medical terms were regarded as “an apparent issue for the prescribing and dispensing of [redacted].” No acronyms/abbreviations related to the prefix/suffix of [redacted] were identified that were regarded as apparent issues for the prescribing/dispensing of [redacted].

#### ***DMETS Response:***

DMETS also identified Darvocet, Dermabet, and Dovonex as names which could be confused orthographically and phonetically with [redacted]. DMETS disagrees with [redacted] conclusions regarding Dermabet. Dermabet and Dovonex are discussed further in this review. The potential for confusion between [redacted] and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with [redacted] in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, or dosage formulation.

#### 2. Section II – Rx Studies – Prescription Collection

Ten health care professionals (six physicians, two pharmacists, and two nurses) produced verbal and handwritten prescriptions for [redacted]. [redacted] included prescriptions of currently marketed drug names in the prescription studies to provide for a control. Each health care professional provided one verbal and two handwritten (inpatient and outpatient) prescriptions for every test name, including [redacted].

#### 3. Section III - Rx Studies – Interpretation and Safety Surveys

[redacted] solicited 240 U.S. health care professionals to interpret the prescriptions. Eighty health care professionals were assigned to each group (Verbal, Handwritten - Inpatient, or Handwritten - Outpatient). Once the health care professionals have interpreted the prescriptions, they complete self-administered questionnaires. The health care professionals were asked to identify proprietary or nonproprietary drug names that may sound like and/or look like the proposed proprietary name.

In the verbal prescription study (n=80), [redacted] was not misinterpreted for any existing brand/generic drug name. In the handwritten inpatient prescription study (n=80), 72 of 80 health care professionals did not misinterpret [redacted] for any existing brand/generic name. The remaining eight professionals misinterpreted the name as Darvocet. In the handwritten outpatient prescription study (n=80), 77 of 80 health care professionals did not misinterpret [redacted] for any existing brand/generic name. The remaining three professionals misinterpreted the name as Darvocet. [redacted] stated that "concern is decreased because Darvocet shares no commonalities with the test product. Additionally, Darvocet is no longer marketed, and no therapeutic equivalents are available." Additionally, nine names were identified as having similar sound and/or look-alike similarities with [redacted] and were further evaluated by [redacted] Safety Evaluators. These nine names were Aldomet, Caduet, Darvocet, Darvon, Daypro, Diabeta, Diovan, Dolobid, and Dovonex. [redacted] concluded that when compared to [redacted] minimal overlapping drug product characteristics were identified that would contribute to a medication error.

**DMETS Response:**

DMETS also identified Darvocet, Dermabet, and Dovonex as names which could be confused orthographically and phonetically with [redacted]. DMETS disagrees with DSI's conclusions regarding Dermabet and Dovonex. Dermabet and Dovonex are discussed further in this review. The proprietary name "Darvocet" (which lacks a modifier) is no longer marketed, however, the Darvocet product line is comprised of Darvocet-N 50 (50 mg/325 mg), Darvocet A500 (100 mg/500 mg), and Darvocet-N 100 (100 mg/650 mg), which are still marketed. The potential for confusion between [redacted] and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with [redacted] in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage formulation.

4. Section IV – Computerized Orthographic and Phonologic Analysis (COPA)

[redacted] conducted a computerized orthographic and phonologic analysis to evaluate the degree of look-alike (orthographic) and sound-alike (phonologic) similarity for all drug names identified in the research relative to [redacted], including drug names originating from all sections of the [redacted] study.

The names Darvocet, Darvocet-N, Darvon, Darvon-N, and Diabeta were found to exceed overall similarity threshold values in the COPA results. [redacted] concluded that when compared to [redacted] minimal overlapping drug product characteristics were identified that would contribute to a medication error.

**DMETS Response:**

DMETS also identified Darvocet as a name which could be confused orthographically and phonetically with [redacted]. The potential for confusion between [redacted] and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with [redacted] in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency

of administration, route of administration, and dosage formulation.

DMETS notes that in addition to the names stated above (Darvocet, Darvocet-N, Darvon, Darvon-N, and Diabeta) as exceeding the overall similarity threshold values, the names Dermabet and Dovonex also exceeded the threshold values in the orthographic results. Dermabet and Dovonex have similar product characteristics with [redacted] and thus we think the potential for confusion is increased.

5. Section V - [redacted] Reference Comparative Safety Analysis

The [redacted] Reference Comparative Safety Analysis provided a side-by-side comparison of the test product's attributes versus those of the marketed products that were identified as being potentially similar by the [redacted] Expert Panel Discussion, healthcare professional survey inputs, prescription studies, and COPA (Study Sections I through IV).

Results of [redacted] Reference Comparative Safety Analysis identified four products, Del-Beta, Dermabet, Dovonex, and Ultravate, which shared three or more commonalities with [redacted]

**DMETS Response:**

DMETS acknowledges the [redacted] Comparative Safety Analysis and considers two of the names (Del-Beta and Ultravate) to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with [redacted], in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage formulation. However, DMETS does not agree with the conclusions of the study regarding the proprietary names Dermabet and Dovonex. Dermabet and Dovonex are discussed in this review.

6. Section VI - External Advisory Committee (EAC)

Eight health care practitioners on the External Advisory Committee with experience in adverse events, patient safety, and/or risk management reviewed the proposed proprietary name, [redacted] and identified any potential sound-alike and/or look-alike names of marketed drug products.

The External Advisory Committee identified three names, Diovan, Darvocet, and Diabeta, as having similar sound and/or appearance to [redacted]. The EAC concluded that when compared to [redacted], minimal overlapping drug product characteristics were identified that would contribute to a medication error. The EAC found the proposed proprietary name to be an acceptable candidate for the proposed product.

**DMETS Response:**

DMETS also identified Darvocet as a name which could be confused orthographically with [redacted]. The potential for confusion between [redacted] and Darvocet is considered minimal due to the presence of a strength or modifier on prescriptions for Darvocet. DMETS considers the remaining names to have low potential for confusion with [redacted] due to a lack of convincing look-alike/sound-alike similarities with [redacted] in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage formulation.

The [redacted] included that "The results of the [redacted] research favorably supports the use [redacted] as a proposed proprietary name for LEO Pharm's proposed product for psoriasis vulgaris."

**Conclusion:**

DMETS does not agree with the overall conclusions of the "Proprietary Name Safety Assessment" regarding the proprietary name [redacted]. We remain concerned with the look-alike/sound-alike similarities with Dermabet, in addition to the overlapping product characteristics which include; active ingredient (betamethasone), indication for use (psoriasis), frequency of administration (once daily), and route of administration (topical). Additionally, we remain concerned with the look-alike similarities with Dovonex, in addition to the overlapping product characteristics which include; active ingredient (calcipotriene), prescriber population (dermatologists), ordered quantity (30 grams, 60 grams, and 100 grams), treatment duration (chronic), product strength (0.005%), indications for use (psoriasis), route of administration (topical), dosage formulation (ointment), and patient population (psoriasis patients).

C. CONSIDERATION OF [redacted]

DMETS does not recommend the use of the proprietary name, [redacted]. In reviewing the proprietary name, the primary concerns related to look-alike and/or sound-alike confusion with Dermabet and Dovonex.

1. [redacted] may look similar to Dermabet when scripted. Dermabet is a currently marketed prescription topical steroid cream containing Betamethasone Valerate, one of the two drugs also contained in [redacted]. Dermabet is used to treat topical steroid responsive dermatoses, including psoriasis. Dermabet is applied one to three times a day to the affected area. The two names have orthographic similarities including the same word length (8 letters), the same beginning letter [redacted] and the same prefix [redacted]. The middle portion of the name [redacted] in [redacted] may also look like the middle portion of the name '-erma-' in Dermabet, especially if the [redacted] in the letter [redacted] is left off or lacks prominence, or if the name is not scripted clearly (see below). Additionally, both Dermabet and [redacted] are available in only one strength and one dosage formulation, thus it is possible that the product strength and formulation will be omitted on an order and a product will still be dispensed. Furthermore, topical products are often prescribed with "as directed" directions for use. Thus, lack of a differentiating product strength, dosage formulation, or directions for use included on a prescription order may not help to differentiate between the two names. Furthermore, the two names Dermabet and [redacted] have multiple overlapping product characteristics such as; active ingredient (betamethasone), indication for use (psoriasis), frequency of administration (once daily), route of administration (topical), prescriber population (dermatologists), ordered quantity (15 grams), and treatment duration (chronic). Therefore, due to strong orthographic similarities, as well as numerous overlapping product characteristics, DMETS does not believe that these two products should co-exist in the marketplace due to the potential for confusion.

*Dermabet*

2. \_\_\_\_\_ can look similar to Dovonex when scripted. Dovonex is indicated for the treatment of moderate plaque psoriasis and is available in 0.005% ointment, 0.005% cream, and 0.005% solution. Dovonex is applied to affected area(s) twice daily. Dovonex contains Calcipotriene as the single active ingredient while \_\_\_\_\_ contains Calcipotriene in combination with the corticosteroid Betamethasone. The similar beginning letters shared between Dovonex and \_\_\_\_\_, “Dovo” vs. \_\_\_\_\_, is the principal contribution to the look-alike similarities of the two names. Furthermore, the letter “x” in Dovonex can look similar to the letter \_\_\_\_\_, depending on how it is scripted (see sample below).

*Dovonex*

However, \_\_\_\_\_ contains the upstroke letter “x” which, if scripted prominently, may help differentiate the names orthographically. Dovonex is supplied in multiple dosage forms (ointment, cream, and solution). Thus, the intended dosage form will either be stated on the order or obtained from the prescriber prior to dispensing. This dosage form designation will help to differentiate the two names on a prescription and help to minimize the potential for medication errors. However, both products are available as ointments and thus, inclusion of this dosage form on an order may not help to minimize the confusion between the name pair. While the frequency of application (twice daily vs. once daily) is another product characteristic that may help to distinguish Dovonex from \_\_\_\_\_, it is not unlikely to have topical products ordered with “as directed” directions for use. Therefore, even though Dovonex and \_\_\_\_\_ have different dosing frequencies, this product characteristic may not help distinguish between the two names on an order that is written with “as directed” directions for use. Thus, a prescription written for “Dovonex Oint., 30 grams or 1 tube, apply as directed” may be misinterpreted as “\_\_\_\_\_ Oint., 30 grams or 1 tube, apply as directed” and vice versa. If \_\_\_\_\_ is inadvertently dispensed instead of Dovonex, the patient would be exposed a high potency corticosteroid (i.e., betamethasone dipropionate) and may experience the local (e.g., atrophy and hypopigmentation) and systemic (e.g., hypothalamic-pituitary-adrenal axis (HPA) suppression) adverse effects associated with topical corticosteroids. If Dovonex is inadvertently dispensed instead of \_\_\_\_\_, the patient will not receive the benefits of the corticosteroid the prescriber intended the treatment to include and thus, the patient’s condition may fail to improve or worsen. Furthermore, whether the drugs are stored by proprietary name or by route of administration (topical), they will likely be stored next to each other on pharmacy shelves. This may lead to selection errors among these products due to their similar names. Moreover, Dovonex and \_\_\_\_\_ have many overlapping product characteristics including prescriber population (dermatologists), ordered quantity (30 grams, 60 grams, and 100 grams), treatment duration (chronic), product strength (0.005%), indication for use (psoriasis), route of administration (topical), dosage formulation (ointment), and patient population (patients with psoriasis). The orthographic similarities, overlapping product characteristics, and potential for similar prescribing directions (use as directed), increase the potential for confusion involving this name pair. Thus, DMETS does not believe that these two products should co-exist in the marketplace due to the potential for confusion.

D. CONSIDERATION OF TACLONEX

DMETS has no objections to use of the second alternate proprietary name, Taclonex.

Appendix A. DMETS prescription study results for Daivobet

<b>Outpatient</b>	<b>Inpatient</b>	<b>Voice</b>
Daivobet	Darvobet	Davabet
Daivobet	Dauibobit	Davabet
Daivoliet	Darvobit	Davabent
Daivolet	Darvocet	Davobet
Daivolet	Darvo??t	Davabid
Daivobet	Darvobit	Davobed
Daivolet	Daivobet	Davabet
Daivobet	Darvobit	Davabet
Daivobet	Dawobit	Davibed
Daivolet	Darvobit	Daivabet
Daivobet	Dairobet	Davibid
Darvocet	Davobet	Davobet
Daivolet	Dawabit	Davobed
Davolet	Darvobit	Dayvabet
Daivobet	Darvobet	Davabet
Daivolet	Dariobet	Davobet
Daivoliet	Dawobit	Davabet
Daivolet	Daivolet	Davobet
Daivobet (This looks like Darvocet when written. However the cream part is distinguishing)	Davubed	
Daivoliet (Comment: Looks a lot like Darvocet, although this is topically applied and that is orally ingested)	Dawobit	

Appendix B. DMETS prescription study results for Taclonex

<b>Voice</b>	<b>Outpatient</b>	<b>Inpatient</b>
Taclonex	Taelonex	Taclonex
Taclonex	Taclonex	laclonex
Taclonex	Taelonex	Taclonex
Taclonex	Taelonex	Toclonex
Taclonex	Taclonex	Taclonex
Tacklonex	Taelmex	Jaclonex
Taclonex	Taelonex	laclonex
Haplonex	Taclonex	Taclonex
Taquinex	Taelmex	Taelmex
Taclonex	Taclonex	Taclonex
Taclonex	Tallinex	Jaclonex
Taclonex	Taclonex	Taclonex
Tacquinex	Taclonex	Jaclonex
Taclonex	Tollonex	Taclonex
	Taelonex	Jaclonex
	Taclonex	Jaclonex
	Taclonex	Taclonex
	Taclonex	Taclonex
	Toelonea	Laclonex
	Tallvenox	
	Taelonex	

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/s/  
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Laura Pincock  
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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 27, 2005

**NDA#:** 21-852

**NAME OF DRUG:** Dovobet® (Calcipotriene and Betamethasone Ointment) 0.005%/0.05%

**NDA HOLDER:** LEO Pharmaceutical Products Ltd.

**I. INTRODUCTION:**

This consult was written in response to a request from the Division of Dermatology and Dental Drug Products (HFD-540), for assessment of the proprietary name, Dovobet®, regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

**PRODUCT INFORMATION**

Dovobet® is a topical vitamin D analogue/corticosteroid combination ointment indicated for the topical treatment of psoriasis vulgaris. Dovobet® should be applied to affected areas once daily. Dovobet® is supplied in 15 gram, 30 gram, 60 gram, and  collapsible tubes. Dovobet® is currently marketed in Canada, Ireland, Italy, the Netherlands, and the United Kingdom with the same indication and strength.

**II. RISK ASSESSMENT:**

The medication error staff of DMETS conducted a search of several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3</sup> for existing drug names which sound-alike or look-alike to Dovobet® 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<sup>4</sup>. The Saegis<sup>5</sup> 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.

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<sup>1</sup> 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.

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> 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.

<sup>4</sup> WWW location <http://www.uspto.gov/tmdb/index.html>.

<sup>5</sup> Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Dovobet. 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 finds the proprietary name, Dovobet, acceptable from a promotional perspective.
2. The Expert Panel identified three proprietary names that were thought to have the potential for confusion with Dovobet. These products are listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified for Dovobet

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Dovobet	Calcipotriene hydrate and betamethasone dipropionate 0.005% ointment	Apply once daily	
Dovonex	Calcipotriene 0.005% ointment, 0.005% cream, 0.005% solution	Apply twice daily	LA/SA
Dolobid	Diflunisal 250 mg, 500 mg tablets	500 mg to 1,500 mg daily in two or three divided doses	LA/SA
Darvocet	Propoxyphene napsylate and acetaminophen 50 mg/325 mg, 100 mg/500 mg, 100 mg/650 mg tablets	1 to 2 tablets every four hours as needed	LA/SA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

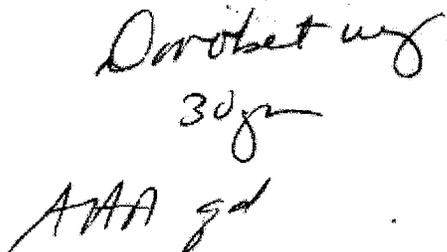
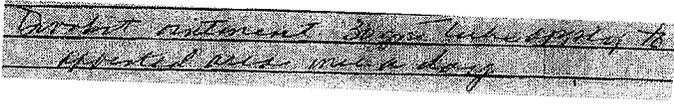
B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

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. All names considered to have significant phonetic or orthographic similarities to Dovobet were discussed by the Expert Panel (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 Dovobet 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 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 Dovobet (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
<p>Outpatient RX:</p> 	<p>Dovobet Ointment 30 gram tube Apply to affected area once a day</p>
<p>Inpatient RX:</p> 	

2. Results:

One respondent from the verbal study misinterpreted the proposed name as Doxepin, an approved product currently marketed in the United States. Additionally, one respondent from the outpatient study misinterpreted the proposed name as "Darvobet", which may look and sound similar to the currently marketed opioid analgesic product, Darvocet. See Appendix A (page 12) for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Dovobet, the primary concerns related to look-alike and sound-alike confusion with Dovonex, Dolobid, and Darvocet.

3. Darvocet can look like Dovobet when scripted. Darvocet, a combination product composed of acetaminophen and the mild narcotic analgesic propoxyphene, is indicated for the relief of mild to moderate pain. Darvocet is supplied as Darvocet-N 50 (50 mg/325 mg), Darvocet A500 (100 mg/500 mg), and Darvocet-N 100 (100 mg/650 mg). The usual adult dose is one to two tablets every four hours as needed. Orthographic similarities may be attributed to endings, “-vocet” vs. “-vobet”, which can look alike when scripted in cursive (see sample below).

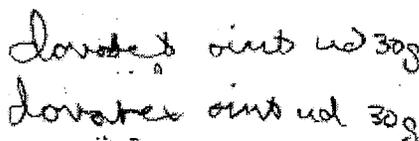


Additionally, both names begin with the letter ‘d’ and the letter “a” in Darvocet can look like the first letter “o” in Dovobet. However, the upstroke characteristic of the letter in Dovobet may help the names look different if scripted prominently. Since Darvocet is available in multiple strengths, the strength of Darvocet must be indicated by use of the modifier or by writing out the strength (e.g., Darvocet-N 100 or Darvocet 100 mg/650 mg). The necessary inclusion of the modifier or strength will help to differentiate Darvocet from Dovobet on a prescription order. Furthermore, the dose written for Darvocet will likely include at least one numeral while the dose for Dovobet will not usually contain any numerals (e.g., 1 to 2 tablets every four hours vs. apply to affected area(s) twice daily). The presence of numerals in the dose on an order for Darvocet may help distinguish these products from one another. DMETS believes the likelihood for confusion between Darvocet and Dovobet is minimal due to the aforementioned reasons.

### III. COMMENTS TO THE SPONSOR:

DMETS does not recommend the use of the proprietary name, Dovobet. In reviewing the proprietary name, the primary concerns related to look-alike and sound-alike confusion with Dovonex.

Dovonex was identified to have look and sound-alike similarities to the proposed name, Dovobet. Dovonex is indicated for the treatment of moderate plaque psoriasis and is available in 0.005% ointment, 0.005% cream, and 0.005% solution. Dovonex is applied to affected area(s) twice daily. Dovonex contains Calcipotriene as the single active ingredient while Dovobet contains Calcipotriene in combination with the corticosteroid Betamethasone. The identical beginning letters shared between Dovonex and Dovobet (“Dovo”) is the principal contribution to the look-alike and sound-alike similarities of the two names. Additionally, the auditory similarities are compounded by the three syllable count and orthographic similarities by the shared seven letter count. Furthermore, the letter “x” in Dovonex can look similar to the letter “t” in Dovobet, depending on how it is scripted (see sample below).



However, Dovobet contains the upstroke letter (“b”) which, if scripted prominently, may help differentiate the names orthographically. Additionally, the differing last syllable (“-nex” vs. “-bet”) may help to distinguish the names from each other when pronounced. Dovonex is supplied in multiple dosage forms (ointment, cream, and solution). Thus, the intended dosage form will either be stated on the order or obtained from the prescriber prior to dispensing. This dosage form designation will help to differentiate the two names on a prescription and help to minimize the potential for medication errors. However, both products are available as ointments and thus, inclusion of the dosage form on an order may not help to minimize the confusion between the name pair. While the frequency of application (twice daily vs. once daily) is another product characteristic that may help to distinguish Dovonex from Dovobet, it is not unlikely to have topical products ordered with “as directed” directions for use. Therefore, even though Dovonex and Dovobet have different dosing frequencies, this product characteristic may not help distinguish between the two names on an order that is written with “as directed” directions for use. Thus, a prescription written for “Dovonex Oint., 30 grams or 1 tube, apply as directed” may be misinterpreted as “Dovobet Oint., 30 grams or 1 tube, apply as directed” and vice versa. If Dovobet is inadvertently dispensed instead of Dovonex, the patient would be exposed a high potency corticosteroid (i.e., betamethasone dipropionate) and may experience the local (e.g., atrophy and hypopigmentation) and systemic (e.g., hypothalamic-pituitary-adrenal axis (HPA) suppression) adverse effects associated with topical corticosteroids. If Dovonex is inadvertently dispensed instead of — the patient will not receive the benefits of the corticosteroid the prescriber intended the treatment to include and thus, the patient’s condition may fail to improve or worsen. Furthermore, whether the drugs are stored by proprietary name or by route of administration (topical), they will likely be stored next to each other on pharmacy shelves. This may lead to selection errors among these products due to their similar names. Moreover, Dovonex and Dovobet have many overlapping product characteristics including prescriber population (dermatologists), ordered quantity (30 grams, 60 grams, and 100 grams), treatment duration (chronic), product strength (0.005%), indication for use (psoriasis), route of administration (topical), dosage formulation (ointment), and patient population (patients with psoriasis). The orthographic similarities, overlapping product characteristics, and potential for similar prescribing directions (use as directed), increase the potential for confusion involving this name pair.

Additionally, DMETS reviewed the container labels, carton and insert labeling from a safety perspective. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

#### A. GENERAL COMMENTS

1. Revise the established name and strength to read as one of the following examples:

a. Dovobet  
(Calcipotriene and Betamethasone Ointment)  
0.005%           

b. Dovobet  
Calcipotriene 0.005%  
and  
Betamethasone             
Topical Ointment



C. CARTON LABELING (15 g, 30 g, 60 g an

1. See General Comments A-1 through A-6.
2. Relocate the route of administration to the front principal display panel.

D. INSERT LABELING

1. See General Comments A-1 through A-6.
2. PRECAUTIONS (Information for Patients)

a.



- b. In accordance with CFR 201.57(f)(2) reprint the “Information for Patients” subsection at the end of the package insert.

3. DOSAGE AND ADMINISTRATION



4. HOW SUPPLIED

Include the established name of this drug product with the first occurrence of the proprietary name in this section.

V. RECOMMENDATIONS:

- A. DMETS does not recommend use of the proprietary name, Dovobet®.
- B. 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.
- C. DDMAC finds the proprietary name, Dovobet, 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 Diane Smith, project manager, at 301-827-1998.

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Division of Medication Errors and Technical Support  
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Concur: \_\_\_\_\_  
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Team Leader  
Division of Medication Errors and Technical Support  
Office of Drug Safety

Appendix A. DMETS prescription study results for Dovobet

<b>Inpatient</b>	<b>Voice</b>	<b>Outpatient</b>
Dermabet	Dalbavac	Dovobet
Devolert	Davobet	Darobet
Divabit	Dobobax	Darvobet
Divabit	Dobovac	Davobet
Divabit	Dolobat	Davobet
Divobit	Dolobed	Davobet
Divobit	Dovabac	Davobet
Divobit	Dovabak	Dermobet
Divobit	Dovabat	Devobet
Divobit	Dovabec	Dinobet
Divobit	Dovabeck	Dirbst
Divobort	Dovabek	Divoket
Divolent	Dovabet	Dorobet
Dovobet	Dovabet	Dorobet
Dovobet	Dovabet	Dovaket
Dovobit	Dovabet	Dovobet
Dovobit	Dovapex	Dovobet
Dovobit	Dovebet	Dovobet
Dovobit	dovibat	Dovobet
Drobit	Dovobed	Dovobet
Duobit	Dovobet	Dovobet
Duvobit	Doxepin	Dovobet
Dvalort	Govabet	Dovobet
	goverbet	Dovobet
	Govobet	Drobet
	Zovibec	Durobet
	Govobet	

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/s/

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